ACTIVE NATIONAL RESEARCH SERVICE AWARD (NRSA) FELLOWSHIPS

FISCAL YEAR 1998

Henry Khachaturian, Ph.D.
Training Director

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NATIONAL INSTITUTE OF MENTAL HEALTH
ACTIVE INDIVIDUAL NATIONAL RESEARCH SERVICE AWARD (NRSA) FELLOWSHIPS
FISCAL YEAR 1998

FELLOWSHIP MECHANISMS

Individual Predoctoral National Research Service Award for M.D./Ph.D. Fellowships (F30)

National Research Service Award for IndividualPredoctoral Fellowships (F31)

National Research Service Award for Individual Postdoctoral Fellows (F32)

NIMH FUNDING UNITS

Division of Basic and Clinical Neuroscience Research (DBCNR)

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MILLER	DAVID	RUTGERS THE STATE UNIV NEWARK	F31	NMDA RECEPTOR FUNCTION IN NEUROCHEMISTRY OF PARKINSONISM	DBCNR
MINER	LEEANN	UNIVERSITY OF PITTSBURGH AT PITTSBURGH	F32	MONOAMINE INTERACTIONS IN THE PREFRONTAL CORTEX	DBCNR
MORGAN	PETER	MOUNT SINAI SCHOOL OF MEDICINE OF CUNY	F30	PEPTIDERGIC MODULATION OF A CENTRAL PATTERN GENERATOR	DBCNR
MULVANEY	JENNIFER	CORNELL UNIVERSITY ITHACA	F32	BIOPHYSICAL ANALYSIS OF A NOVEL NON-NMDA CHANNEL	DBCNR
MYERS	SCOTT	EMORY UNIVERSITY	F31	MECHANISMS OF RAT GLUR2 GENE EXPRESSION IN NEURONS	DBCNR
NAIR	HEMANTH	UNIVERSITY OF TEXAS AUSTIN	F31	BRAIN IMAGING OF DEVELOPMENTAL LEARNING EFFECTS	DMDBA
NAKAMURA	KEN	UNIVERSITY OF CHICAGO	F30	GLUTATHIONE AND DOPAMINERGIC NEURONAL SURVIVAL	DBCNR
NEMANIC	SARAH	UNIVERSITY OF TEXAS HLTH SCI CTR HOUSTON	F31	ANIMAL VISUAL, SPATIAL, AND CONTEXTUAL LEARNING/MEMORY	DBCNR
NETOFF	THEODEN	GEORGE MASON UNIVERSITY	F31	DEFECTING GENERALIZED SYNCHRONY OF CELLS IN HIPPOCAMPUS	DBCNR
NETT	SHOLEEN	DARTMOUTH COLLEGE	F30	SEXUAL DIMORPHISM IN HYPOTHALAMIC SYNAPTIC TRANSMISSION	DBCNR
NOELLE	DAVID	CARNEGIE-MELLON UNIVERSITY	F32	NEUROCOMPUTATION OF EXPLICIT LEARNING FROM INSTRUCTION	DMDBA
OBRIETAN	KARL	UNIVERSITY OF WASHINGTON	F32	ADENYLYL CYCLASES AND CIRDADIAN RHYTHM	DBCNR
OCHSNER	KEVIN	HARVARD UNIVERSITY	F32	SOCIAL COGNITIVE NEUROSCIENCE APPROACH--RATIONALIZATION	DMDBA
ORLANDO	LIANNA	MASSACHUSETTS GENERAL HOSPITAL	F31	METABOTROPIC RECEPTORS AND EFFECTORS IN EXCITOTOXICITY	DBCNR
OTMAKHOVA	NONNA	BRANDEIS UNIVERSITY	F32	MECHANISMS OF D1 DOPAMINE ENHANCEMENT OF EARLY LTP	DBCNR
PAGE	WILLIAM	UNIVERSITY OF ROCHESTER	F31	NEURONAL RESPONSES TO SELF-MOTION DURING SMOOTH PURSUIT	DBCNR

PALADINI	CARLOS	RUTGERS THE STATE UNIV NEWARK	F31	AFFERENT REGULATION OF NIGRAL DOPAMINERGIC NEURONS	DBCNR
PARK	JAE	BRANDEIS UNIVERSITY	F32	NEUROENDOCRINE REGULATION OF THE CIRCADIAN RHYTHMS	DBCNR
PATRICK	TODD	UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN	F30	ENGINEERED BISPECIFIC ANTIBODY TARGETING OF BRAIN TUMORS	DBCNR
PELLEGRINO	TRISHA	GEORGETOWN UNIVERSITY	F31	IMMUNOMODULATORY EFFECTS OF SEROTONIN UPTAKE INHIBITORS	DBCNR
PENNELL	NATHAN	UNIVERSITY OF FLORIDA	F31	MICROGLIA AND NEURAL TRANSPLANTATION	DBCNR
PETRULIS	ARAS	BOSTON COLLEGE	F32	PHYSIOLOGY OF INDIVIDUAL DISCRIMINATION/RECOGNITION	DBCNR
PHILLIPS	LYNNETTE	BRIGHAM AND WOMEN'S HOSPITAL	F32	SITE SPECIFIC REGULATION OF IMMUNE FUNCTION IN THE CNS	DBCNR
PIEPER	ANDREW	JOHNS HOPKINS UNIVERSITY	F30	IN VIVO MODULATION OF THE IP3R BY PHOSPHORYLATION	DBCNR
PIERCHALA	BRIAN	JOHNS HOPKINS UNIVERSITY	F31	RETROGRADE NEUROTROPHIN SIGNALING	DBCNR
PIETRAS	CYNTHIA	UNIVERSITY OF FLORIDA	F31	HUMAN CHOICE IN SITUATIONS OF UNCERTAINTY AND RISK	DMDBA
PLAUTZ	ERIK	UNIVERSITY OF TEXAS HLTH SCI CTR HOUSTON	F31	LEARNING-DEPENDENT ALTERATIONS IN PRIMATE MOTOR CORTEX	DBCNR
POWELL	SUSAN	UNIVERSITY OF FLORIDA	F31	STRESS RESPONSIVENESS IN ABNORMAL REPETITIVE BEHAVIOR	DBCNR
PRABHAKARAN	VIVEK	STANFORD UNIVERSITY	F30	BASAL GANGLIA AND WORKING MEMORY	DBCNR
PRATT	WAYNE	UNIVERSITY OF UTAH	F31	SPACE AND REWARD INTEGRATION IN THE NUCLEUS ACCUMBENS	DBCNR
PRICE	KIMBERLY	UNIVERSITY OF WISCONSIN MADISON	F32	STRESS, PRENATAL VACCINATION AND INFANT IMMUNITY	DBCNR
PRICE	MICHELLE	UNIVERSITY OF PENNSYLVANIA	F31	CORTICOTROPIN-RELEASING FACTOR AND SEROTONIN INTERACTION	DBCNR

PRINSTEIN	MITCHELL	RHODE ISLAND HOSPITAL (PROVIDENCE, RI)	F32	SOCIAL FUNCTIONING AND SUICIDALITY ACROSS DEVELOPMENT	DMDBA
PRYBYLOWSKI	KATE	GEORGETOWN UNIVERSITY	F31	TYROSINE PHOSPHORYLATION AND NMDA RECEPTOR FUNCTION	DBCNR
PUGH	C	UNIVERSITY OF COLORADO AT BOULDER	F31	SELECTIVE CYTOKINE EFFECTS ON LEARNING/MEMORY PROCESSES	DBCNR
QUELLER	SARAH	PURDUE UNIVERSITY WEST LAFAYETTE	F32	CONNECTIONIST MODELS AND PERCEPTIONS OF ATYPICAL GROUP M	DMDBA
QUIRK	JENNIFER	DUKE UNIVERSITY	F31	CALCIUM ACTIVATED K CHANNEL ASSOCIATION DOMAINS	DBCNR
RAGOZZINO	MICHAEL	UNIVERSITY OF UTAH	F32	MNEMONIC PROPERTIES OF THE PREFRONTAL CORTEX	DBCNR
RALPH	REBECCA	UNIVERSITY OF CALIFORNIA SAN DIEGO	F31	DOPAMINE MODULATION OF PPI AND LMA IN KNOCKOUT MICE	DBCNR
RAMUS	SETH	BOSTON UNIVERSITY	F32	HIPPOCAMPAL DEPENDENT CORTICAL MEMORY REPRESENTATION	DBCNR
REBER	PAUL	UNIVERSITY OF CALIFORNIA SAN DIEGO	F32	NEUROPSYCHOLOGICAL STUDIES OF IMPLICIT MEMORY	DMDBA
REPA	J	NEW YORK UNIVERSITY	F31	PLASTICITY IN SENSORY INPUT PATHWAYS TO THE AMYGDALA	DBCNR
REYES	TERESA	UNIVERSITY OF WISCONSIN MADISON	F31	CYTOKINE CASCADE--A PATHWAY TO THE BRAIN	DBCNR
RHEN	TURK	UNIVERSITY OF TEXAS AUSTIN	F31	EVOLUTION AND BEHAVIORAL ORGANIZATION	DBCNR
ROGERS	RONALD	INDIANA UNIVERSITY BLOOMINGTON	F32	NEURAL CORRELATES OF CONTEXTUAL-BASED LEARNING	DBCNR
ROSENTHAL	SAUL	UNIV OF MED/DENT NJ-R W JOHNSON MED SCH	F32	SOCIAL RESPONSIBILITY AND THE DEVELOPMENT OF COMPETENCE	DMDBA
ROTH	JONATHAN	UNIVERSITY OF FLORIDA	F31	DUAL ANORECTIC TREATMENT IN RATS--EFFICACY AND SAFETY	DBCNR
ROUSE	SUSAN	EMORY UNIVERSITY	F32	MUSCARINIC ACTYLCHOLINE RECEPTORS IN PERFORANT PATHWAY	DBCNR

SAEZ	EMILY	UNIVERSITY OF PUERTO RICO RIO PIEDRAS	F31	FAMILY ENVIRONMENT AND DEPRESSION IN ADOLESCENTS	DMDBA
SAGE	JENNIFER	UNIVERSITY OF CALIFORNIA LOS ANGELES	F31	MNEMONIC FUNCTIONS OF THE BASAL GANGLIA	DMDBA
SAILSTAD	CYNTHIA	MOUNT SINAI SCHOOL OF MEDICINE OF CUNY	F31	NEURAL MECHANISMS CONTROLLING RECEPTIVE FIELD PARAMETERS	DBCNR
SALAT	DAVID	OREGON HEALTH SCIENCES UNIVERSITY	F31	FRONTAL LOBE ATROPHY IN ALZHEIMERS DISEASE AND AGING	DBCNR
SALO	RUTH	UNIVERSITY OF CALIFORNIA DAVIS	F32	FRONTAL LOBE AND SEQUENTIAL PROCESSES IN SCHIZOPHRENIA	DMDBA
SAMUELSON	LARISSA	INDIANA UNIVERSITY BLOOMINGTON	F31	EARLY WORD LEARNING--COMPUTATIONAL AND BEHAVIORAL TESTS	DMDBA
SANGORAM	ASHVIN	NORTHWESTERN UNIVERSITY	F30	CIRCADIAN RHYTHMS IN CLOCK KNOCKOUT MICE	DBCNR
SAVASTANO	HERNAN	STATE UNIVERSITY NEW YORK BINGHAMTON	F32	CONTEXT AND TIMING ON ASSOCIATIVE LEARNING	DMDBA
SCHAFE	GLENN	NEW YORK UNIVERSITY	F32	CREB LTP AND FEAR MEMORY	DBCNR
SCHELL	MICHAEL	UNIVERSITY OF CAMBRIDGE	F32	FUNCTIONAL AND PATHOLOGIC ROLES OF GAP1 IP4BP IN BRAIN	DBCNR
SCHIML	PATRICIA	UNIVERSITY OF VIRGINIA CHARLOTTESVILLE	F32	NEUROBEHAVIORAL ADAPTATIONS, HORMONES, AND STRESS	DBCNR
SCHMADER	TANYA	UNIVERSITY OF CALIFORNIA SANTA BARBARA	F31	DIFFERENTIATING SELF FROM GROUP--IS IT SELF PROTECTIVE	DMDBA
SCHRAUF	ROBERT	DUKE UNIVERSITY	F32	CULTURAL EFFECTS ON RETENTION IN AUTOBIOGRAPHICAL MEMORY	DMDBA
SCHULTZ	LAURA	SALK INSTITUTE FOR BIOLOGICAL STUDIES	F32	CALCIUM DYNAMICS IN HIPPOCAMPAL CA1 INTERNEURONS	DBCNR
SHARKEY	KATHERINE	RUSH UNIVERSITY	F30	PHASE SHIFTING AND SEDATIVE EFFECTS OF MELATONIN	DBCNR
SHERFF	CAROLYN	YALE UNIVERSITY	F32	CELLULAR ANALYSIS OF MEMORY STAGES IN APLYSIA	DBCNR

SHERMAN	SUSAN	JOHNS HOPKINS UNIVERSITY	F31	EXPLORING RISK FACTORS OF HIV AMONG WOMEN	DMDBA
SIBILLE	ETIENNE	CORNELL UNIVERSITY MEDICAL CENTER	F31	NEUROBIOLOGY OF ANXIETY IN 5HT1A KNOCKOUT MICE	DBCNR
SIMERAL	JOHN	WAKE FOREST UNIVERSITY	F31	NONLINEAR SYSTEMS ANALYSIS OF HIPPOCAMPAL ENSEMBLES	DBCNR
SIMS	KAREN	UNIVERSITY OF PENNSYLVANIA	F30	REGULATION OF EAAC1, A NEURONAL GLUTAMATE TRANSPORTER	DBCNR
SMITH	DAVID	UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN	F31	NEURAL MEDIATION OF CONTEXT APPROPRIATE BEHAVIOR	DBCNR
SMOKOWSKI	PAUL	UNIVERSITY OF WISCONSIN MADISON	F31	RISK AND RESILIENCE IN ADOLESCENT MENTAL HEALTH	DMDBA
SOBEL	DAVID	UNIVERSITY OF CALIFORNIA BERKELEY	F31	CAUSAL EXPLANTATION AND CATEGORIZATION IN DEVELOPMENT	DMDBA
SOLOMON	KAREN	NORTHWESTERN UNIVERSITY	F32	NEW INFORMATION EFFECT ON MULTIPLE CATEGORIES	DMDBA
SPENCER	KEVIN	UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN	F31	INTERHEMISPHERIC INTERACTION IN ATTENTION	DBCNR
SPIEGEL	SCOTT	UNIVERSITY OF MARYLAND COLLEGE PK CAMPUS	F31	ACCESSIBILITY EFFECTS IN A UNIMODAL THEORY OF PERSUASION	DMDBA
SRINIVASAN	RAJAGOPAL	EMORY UNIVERSITY	F31	IMAGE ENCODING BY THE PRIMATE LATERAL GENICULATE NUCLEUS	DBCNR
STARK	JENNIFER	OHIO STATE UNIVERSITY	F31	NGF MODULATION OF VIRUS INDUCED INFLAMMATION	DBCNR
STINE	CHRISTY	FINCH UNIV OF HLTH SCI/CHICAGO MED SCH	F30	GLUTAMATE TRANSMISSION IN A RAT MODEL OF SCHIZOPHRENIA	DBCNR
TAFT	CASEY	UNIVERSITY OF MARYLAND BALT PROF SCHOOL	F31	PREDICTING DROPOUT AND CHANGE IN BATTERERS TREATMENT	DMDBA
TALLEY	EDMUND	UNIVERSITY OF VIRGINIA CHARLOTTESVILLE	F31	ANTIDEPRESSANT EFFECTS--CELLULAR/MOLECULAR MECHANISMS	DBCNR
TAN	PHILIP	SCRIPPS RESEARCH INSTITUTE	F32	SORTING OF A MEMBRANE PROTEIN INTO LDCVS	DBCNR

TANNENBAUM	PAMELA	UNIVERSITY OF WISCONSIN MADISON	F32	SOCIAL REGULATION OF REPRODUCTIVE ENDOCRINOLOGY	DBCNR
TAYLOR	AMY	COLUMBIA UNIV NEW YORK MORNINGSIDE	F31	MENTAL MODEL OF FUN AND IMPORTANCE INFLUENCE PERFORMANC	DMDBA
TEKIRIAN	TINA	UNIVERSITY OF KENTUCKY	F31	ENTORHINAL CORTEX PATHOLOGY AND COGNITIVE PERFORMANCE	DBCNR
TENG	EDMOND	UNIVERSITY OF CALIFORNIA SAN DIEGO	F30	HIPPOCAMPUS--SPATIAL AND NONSPATIAL MEMORY FUNCTION	DBCNR
THOMPSON	RICHMOND	OREGON STATE UNIVERSITY	F32	NEUROPEPTIDE INFLUENCES UPON SEXUAL BEHAVIOR	DBCNR
TOMA	DANIEL	UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN	F31	MOLECULAR GENETIC ANALYSIS OF BEHAVIOR	DBCNR
TREUTING	JENNIFER	UNIVERSITY OF CALIFORNIA BERKELEY	F31	PATHWAYS TO DEPRESSIVE SYMPTOMS AMONG CHILDREN WITH ADHD	DMDBA
TSAI	HOUNG	UNIVERSITY OF KENTUCKY	F31	MECHANISM FOR ABOLISHING GONADOTROPIN SURGES BY ESTROGEN	DBCNR
TURNER	MICHAEL	LOYOLA UNIVERSITY MEDICAL CENTER	F30	PALLIDAL GLUTAMATE IN A RAT MODEL OF PARKINSONS DISEASE	DBCNR
TYRKA	AUDREY	UNIVERSITY OF PENNSYLVANIA	F30	NEUROPSYCHOLOGICAL INDICATORS OF RISK FOR SCHIZOPHRENIA	DBCNR
VAIDYA	MANISH	UNIVERSITY OF FLORIDA	F31	DO EQUIVALENCE CLASSES MEDIATE EXTENSIONS OF FUNCTION?	DMDBA
VALERA	EVE	UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN	F31	MINOR HEAD INJURY IN BATTERED WOMEN	DMDBA
VERIN-SHAPIRO	PENNY	CASE WESTERN RESERVE UNIVERSITY	F31	RELIGIOUS HEALING AND IDENTITY IN PUERTO RICO	DMDBA
VICKBERG	SUZANNE	CUNY GRADUATE SCH AND UNIV CTR	F31	ADJUSTMENT TO BREAST CANCER--THE ROLE OF INTERPRETATION	DMDBA
VNEK	NORBERT	YALE UNIVERSITY	F32	FUNCTIONAL MODULARITY OF THE PRIMATE PREFRONTAL CORTEX	DBCNR
VOLLRATH	MELISSA	BAYLOR COLLEGE OF MEDICINE	F31	HAIR CELL TRANSDUCTION IN A MAMMALIAN VESTIBULAR ORGAN	DBCNR

WAINWRIGHT	MARCY	UNIVERSITY OF TEXAS HLTH SCI CTR HOUSTON	F31	MORPHOLOGICAL CORRELATES OF LONG TERM SENSITIZATION	DBCNR
WALTZ	JAMES	UNIVERSITY OF CALIFORNIA LOS ANGELES	F31	INVESTIGATING REASONING DEFICITS IN DEMENTIA PATIENTS	DBCNR
WARD	BONNIE	UNIVERSITY OF ROCHESTER	F31	BRAIN SPACE AND AVIAN VOCAL LEARNING	DBCNR
WEBB	SARA	UNIVERSITY OF MINNESOTA TWIN CITIES	F31	ONTOGENY OF MEMORY--ELECTROPHYSIOLOGICAL EVIDENCE	DMDBA
WEERSING	VANESSA	UNIVERSITY OF CALIFORNIA LOS ANGELES	F31	THERAPY PROCESS CHECKLIST--DEVELOPMENT AND APPLICATION	DSIR
WEIHL	CONRAD	UNIVERSITY OF CHICAGO	F30	VIRAL VECTORS IN THE STUDY OF ALZHEIMERS DISEASE	DBCNR
WEST	JENNIFER	UNIVERSITY OF DENVER	F31	CHILDREN AND MARITAL CONFLICT--LINKS TO SOCIAL BEHAVIOR	DMDBA
WETHERELL	JULIE	UNIVERSITY OF SOUTHERN CALIFORNIA	F31	GENERALIZED ANXIETY DISORDER IN OLDER ADULTS	DSIR
WILLCUTT	ERIK	UNIVERSITY OF COLORADO AT BOULDER	F32	BEHAVIORAL AND MOLECULAR GENETIC STUDY OF ADHD	DMDBA
WILLIAMS	JULIE	MASSACHUSETTS GENERAL HOSPITAL	F32	MELATONIN FUNCTION IN CIRCADIAN RHYTHMS	DBCNR
WILSON	JULIE	UNIVERSITY OF IOWA	F31	HUMAN NEURAL SYSTEMS FOR PERCEIVING EMOTION IN MUSIC	DMDBA
WILSON	WILLARD	UNIVERSITY OF MARYLAND COLLEGE PK CAMPUS	F32	LOCALIZATION AND TRACKING OF MOVING TARGETS BY BATS	DMDBA
WINNIER	ANGELA	VANDERBILT UNIVERSITY	F31	MOLECULAR GENETICS OF THE NEURAL SPECIFICITY GENE BKN-1	DBCNR
WINTERBAUER	NANCY	STATE UNIVERSITY NEW YORK BINGHAMTON	F31	STRESS AND CULTURE CHANGE AMONG THE YUCATEC MAYA	DMDBA
WISOR	JONATHAN	STANFORD UNIVERSITY	F32	DOPAMINE & SLEEP HOMEOSTASIS--MOLECULAR GENETIC APPROACH	DBCNR
WOLF	ROBERT	JOHNS HOPKINS UNIVERSITY	F31	PSYCHOSOCIAL DETERMINANTS FOR HIV RISK BEHAVIORS	DMDBA

WOODS	ALISA	UNIVERSITY OF CALIFORNIA	F31	NEUROCYTOKINES IN REACTIVE HIPPOCAMPAL SPROUTING	DBCNR
WOTRING	VIRGINIA	UNIVERSITY OF ALABAMA AT BIRMINGHAM	F32	KINETIC ANALYSIS OF WILD-TYPE/MUTANT GABA RHO RECEPTORS	DBCNR
WRAGA	MARYJANE	UNIVERSITY OF VIRGINIA CHARLOTTESVILLE	F32	EYE HEIGHT AND SIZE PERCEPTION	DMDBA
WRIGHT	TIMOTHY	UNIVERSITY OF MARYLAND COLLEGE PK CAMPUS	F32	DISCRIMINATION OF NATURAL AND SYNTHETIC CALL VARIANTS	DMDBA
WU	GREGORY	UNIVERSITY OF IOWA	F30	CTL ESCAPE MUTANTS--ROLE IN MHV INDUCED DEMYELINATION	DBCNR
WU	MARK	BAYLOR COLLEGE OF MEDICINE	F31	MUTATIONAL ANALYSIS OF SYNTAXIN 1-A IN VIVO	DBCNR
WURTS	SARAH	STANFORD UNIVERSITY	F31	CIRCADIAN AND HOMEOSTATIC REGULATION OF REM SLEEP	DBCNR
YARALIAN	PAULINE	UNIVERSITY OF SOUTHERN CALIFORNIA	F31	PSYCHOPHYSIOLOGY--AGGRESSION AND HYPERACTIVITY	DMDBA
YECKEL	MARK	BAYLOR COLLEGE OF MEDICINE	F32	ACTIVE PROPERTIES OF DENDRITES OF CA3 PYRAMIDAL NEURONS	DBCNR
YEH	MAY	CHILDREN'S HOSPITAL RESEARCH CENTER	F32	SERVICE DELIVERY TO ASIAN AMERICAN YOUTHS	DSIR
YU-ISENBERG	KRISTINA	JOHNS HOPKINS UNIVERSITY	F31	COMPLIANCE WITH ANTIRETROVIRAL THERAPY IN HIV+ WOMEN	DMDBA
ZALD	DAVID	UNIVERSITY OF MINNESOTA TWIN CITIES	F32	NEURAL CORRELATES OF EMOTION	DBCNR
ZEDDIES	DAVID	NORTHWESTERN UNIVERSITY	F31	ADAPTATION IN RECEPTOR POTENTIALS OF INNER HAIR CELLS	DBCNR
ZEINEH	MICHAEL	UNIVERSITY OF CALIFORNIA LOS ANGELES	F31	FUNCTIONAL MRI OF THE HUMAN HIPPOCAMPUS	DBCNR
ZIEGLER	DANA	UNIVERSITY OF KENTUCKY	F31	GLUTAMATERGIC NEUROCIRCUITRY AND STRESS ACTIVATION	DBCNR
ZYLKA	MARK	MASSACHUSETTS GENERAL HOSPITAL	F31	MOLECULAR ACCESS TO THE MAMMALIAN BIOLOGICAL CLOCK	DBCNR

1F32MH012101-01
ABRAMOWITZ, JONATHAN
SPACING OF SESSIONS IN THE BEHAVIORAL TREATMENT OF OCD
ALLEGHENY UNIVERSITY OF HEALTH SCIENCES
BRYN MAWR, PA

DESCRIPTION (Adapted from applicant's abstract) : Behavior therapy, i.e., exposure and response prevention (E/RP), is considered the psychological treatment of choice for obsessive-compulsive disorder (OCD). This treatment entails 3 weeks of daily 1-2 hour sessions (15 total sessions) in which feared situations are confronted with therapist supervision (exposure), and ritualizing is curtailed (respone prevention). However, because of the large time commitment needed to undertake E/RP, many individuals with OCD are either unable or unwilling to begin treatment. With the specific goals of testing the efficacy and durability of a less intensive E/RP protocol that might decrease treatment refusal rate, we propose a 3 year controlled treatment study to compare 15 sessions of daily E/RP delivered over 3 weeks to 15 sessions delivered twice per week over 7.5 weeks. A mid- treatment assessment (after 8 sessions) will also be included to determine whether fewer sessions of daily treatment are needed to achieve symptom reduction. The patients will be 25 adults with a DSM-IV diagnosis of OCD. The primary outcome measure is the Yale-Brown Obsessive- Compulsive Scale. Assessments conducted by evaluators blind to treatment status will take place at pretreatment, mid-treatment, posttreatment, and three and six month follow-up.

1F32MH012160-01
AHRENS, KURT
NEURAL CORRELATES OF A TRAINED SENSORIMOTOR TASK
UNIVERSITY OF CALIFORNIA SAN DIEGO
LA JOLLA, CALIFORNIA

DESCRIPTION (Adapted from applicant's abstract) : The aim of this project is to measure neural activity in the somatosensory, motor, and limbic brain areas of rat during performance of a behavioral task. Two specific issues that will be investigated are the temporal dynamics of activity in each of these areas at each stage of the behavior and the extent to which they interact. Single unit and field potential data will be acquired by recording from chronically implanted multichannel microelectrodes as the rats rely on the sense of touch, mediated by their whiskers, to choose between cookies whose shapes have either positive or negative associations (i.e., certain shapes will be embittered with an odorless additive). Recordings will be made from the time when the animals are first learning these associations through the time when they are skilled at making discriminations, including occasional reversals of reward contingency and subsequent relearning. Using a variety of analytical methods to related neural and behavioral data should provide insight into the cooperative function of these disparate brain systems as the rat learns how to get a reward and produces goal directed behavior. The broad goal of this research is to engender a deeper understanding of basic cortical function, especially in relation to behavior. Examining the interactions of sensory, motor, and limbic brain areas is a necessary step in the development of an explanatory theory of brain function. With the framework of knowledge provided by studies like this, clinicians may be able to diagnose and develop treatments for ailments involving impaired cortico-cortical signaling. Two areas of application are envisioned: 1) the identification of specific behavioral deficits involving interactions between sensory, motor, and/or limbic areas;

and 2) the theoretically driven identification and treatment of "dynamical diseases" (i.e. diseases whose underlying dynamics are best described by nonlinear mathematics).

5F32MH011103-02
ALBERT,MARC
PERCEPTION OF VISUAL SURFACES
HARVARD UNIVERSITY
Boston Massachusetts

DESCRIPTION (Adapted from Applicant's Abstract) : The perception of visual surfaces is central to the processes by which humans come to understand and control their environment. Tasks such as object recognition, grasping, and manipulation, and path planning and obstacle avoidance require reliable information about surface layout. The aim of this proposal is to study the assumptions used by human vision in its perception of visual surfaces. Particular attention will be focused on the assumption of "generic viewing position": Human vision assumes that the qualitative structure of an image is stable under small changes of viewpoint. The experiments will explore visual surface perception in a range of contexts, including, monocular line- drawings of surfaces, untextured stereo surfaces, and subjective surfaces (such as the Kanizsa triangle). The goal is to clearly delineate the empirical content, scope, and limits of the generic view principle, and to further scientific knowledge about the role of surface organization in 3-D perception.

5F32MH010929-03
ALVARADO,MARIA
HIPPOCAMPAL FORMATION AND PRIMATE MEMORY
UNIVERSITY OF TEXAS HLTH SCI CTR HOUSTON
Houston, Texas

DESCRIPTION (Adapted from Applicant's Abstract):
The proposed research will use selective lesion techniques to assess the role of the hippocampal formation in learning and memory in rhesus monkeys. Specifically- the effects of ibotenic acid induced damage to the hippocampal formation will be compared with those of aspiration lesions of rhinal cortex and transections of the fornix on five behavioral tasks: 1) list learning, as measured by the serial probe recognition task; 2) relational learning, as measured by the transverse patterning problem; 3) spatial learning, as measured by an analog of the radial arm maze; 4) recognition memory, as measured by performance on trial-unique delayed nonmatching-to- sample; 5) concurrent discrimination learning, as measured by the 24 hour intertrial interval task. These experiments are designed to discover what role, if any, the hippocampal formation (or its interaction with cortical and subcortical structures) has to play in the above memory systems.

1F30MH012078-01
ANCES, BEAU
ACTIVATION FLOW COUPLING--MECHANISMS AND MEDIATORS
UNIVERSITY OF PENNSYLVANIA
PHILADELPHIA, PENNSYLVANIA

DESCRIPTION (Adapted from Applicant's Abstract):
Activation-flow coupling is a fundamental aspect of brain physiology and forms the basis of most functional neuroimaging techniques, yet the mechanisms and mediators of activation-flow coupling remain poorly

understood. An improved understanding of these mechanisms and mediators is critical for interpreting functional activation studies in pathological conditions such as Alzheimer's disease, Parkinson's disease, stroke, and schizophrenia. Further, abnormalities in activation-flow coupling may reflect disease-specific pathophysiology and may contribute to differential diagnosis of central nervous system disorders. A rat model system will be developed to characterize activation-flow coupling in the somatosensory cortex in response to electrical forepaw stimulation. Laser Doppler (LD) recordings will be used to characterize changes in velocity, volume, and calculated rCBF in alpha- chloralose anesthetized rats in response to parametric variations in frequency, amplitude, and duration of stimulus. LD has the advantage of being able to monitor changes in rCBF with high temporal resolution and minimal invasiveness. An increase in the signal to noise ratio and reproducibility of LD measurements will be enhanced by using the novel approach of digital signal averaging of recorded responses. The effects of pharmacological manipulation on activation-flow coupling will also be examined. Pharmacological agents that will be administered include the adenosine antagonist- theophylline; a neuronal nitric oxide synthase inhibitor- 7-NINA; a neuronal and endothelial nitric oxide synthase inhibitor - L-NAME; and a NMDA antagonist- MK-801. It is hoped that the establishment of this rat model system and the application of different agents to this system will provide clues as to whether activation-flow coupling is mediated both by neurogenic and metabolic factors.

5F31MH11364-02
ANGELL, KATHRYN E
SEX DIFFERENCES IN DEPRESSION? COLLEGE V 18-22 AGE GROUP
UNIVERSITY OF WISCONSIN MADISON
MADISON, WISCONSIN

DESCRIPTION (Candidate's Abstract) : Research on unipolar depression currently lacks a clear demonstration of the etiology and a thorough understanding of the 2:1 ratio for depression in women versus men. An explanation of this central phenomenon of depression and identification of the causal factors which produce this striking gender difference would greatly advance depression research. Clearly, understanding why women are more vulnerable to depression than men would also promote better clinical techniques by focusing attention on potent vulnerability factors and facilitating early treatment or prevention of depression. The small enigmatic literature on whether or not gender differences in depression exist in college student samples contains mixed evidence and does not address whether the suggested lack of gender differences applies only to college research samples or to the entire age group. This information is crucial for the correct interpretation of the large body of depression literature which uses college research samples. In addition, if college research samples do not show gender differences in depression, this fact may help elucidate why other adult age group do show these gender differences. The proposed study makes the key comparison between a typical college research sample and a multi-site 1822 year old community sample for depressive symptoms and current as well as lifetime histories of major and minor depressive episodes.
Furthermore, it measures potential causal mechanisms proposed by the diverse areas of cognitive theories of depression, response styles theory, and alcohol use and abuse. If the two samples differ with respect to the presence of gender differences in depression, multivariate analyses of variance and multiple regression will be used to assess the ability of each proposed etiological mechanism to mediate gender differences in depression.

1F32MH012161-01
ANTIC, SRDJAN
SIGNAL INTEGRATION IN THE MITRAL NEURON
YALE UNIVERSITY
NEW HAVEN, CONNECTICUT

DESCRIPTION (Adapted from applicant's abstract) : The main objective of this proposal is to investigate by direct measurement how individual mitral neurons are functionally organized and incorporate the results in a compartmental model of the mitral nerve cell. The long-term goal is to use the information about individual nerve cells as the basis for an understanding of how networks of interconnected neurons operate to control behavior. In the long run, the knowledge we obtain about how normal behavior is generated will help us understand mental disorders such as depression, drug addiction or schizophrenia. Understanding how single neurons process information is fundamental to understanding how the brain works. A complete understanding of any individual cell's function has not yet been obtained. Due to linear and nonlinear membranes, the regional electrical properties of branching processes are complex and impossible to predict in the absence of spatially resolved measurements. The experiments will be carried out to characterize in detail one exemplar neuron, the mitral neuron in the rat olfactory bulb. We will try to look at the processing of excitatory (from olfactory nerve) and inhibitory inputs (from granule cells), in the most direct way, by optical monitoring of membrane potential transients at many sites by using intracellular voltage sensitive dyes. We plan to determine the number and locations of trigger zones and to determine whether dendrites are capable of generating spikes. We are going to test experimentally the hypothesis that besides the apical (primary) dendrite the back propagation, also occurs in tuft and secondary dendrites to influence synaptic plasticity. We also plan to test the hypothesis that individual neurons can be functionally subdivided. If true, this postulate would have important implications for the functional complexity of individual neurons.

1F31MH011919-01
ARNDT, MICHELLE
ORPHANIN FQ--A NOVEL NEUROENDOCRINE FUNCTION
WEILL MEDICAL COLLEGE OF CORNELL UNIV
ITHACA, NEW YORK

DESCRIPTION (Adapted from applicant's abstract) : The long term objective of this proposal is to understand the cellular mechanisms of the opioid-like peptide orphanin FQ (OFQ) in the anterior pituitary corticotroph tumor cell line AtT-20. My specific aims are: (1) To demonstrate that OFQ can interact specifically at the ORL-1 (Opioid Receptor-like 1) to stimulate release of ACTH from AtT-20 cells. This will be accomplished by measuring ACTH secretion from AtT-20 cells in response to OFQ. ORL-1 mRNA will be measured and binding studies conducted to confirm the presence of ORL-1 in AtT-20 cells. There is no known antagonist for ORL-1, thus antisense will be used to determine if OFQ is acting specifically through ORL-1. (2) To demonstrate that OFQ-stimulated ACTH secretion occurs via a G-protein coupled mechanism which involves an increase in inositol phosphate (IP) levels and (Ca2+)i. This will be accomplished by measuring IP stimulation from AtT-20 cells in response to OFQ. The effects of GTP- gammaS and GDP-betaS on OFQ-stimulated IP secretion will be examined, as well as the effects of pertussis toxin. In addition, the effects of Ca2+ channel

blockers including nifedipine and omega- conotoxin on IP and ACTH production will be determined. The role of internal Ca2+ stores in OFQ-stimulated ACTH secretion will also be examined by treating cells with thapsagargin or ryanodine. OFQ has not previously been shown to increase levels of IPs in any cell system, nor has the role of OFQ in neuroendocrine secretion been examined. An understanding of the regulatory role of OFQ in neuroendocrine secretion may be potentially very useful in the treatment of hormonal disorders, or, conversely, OFQ may produce adverse effects on neuroendocrine function. The studies proposed here will greatly enhance our understanding of the role of OFQ in neuroendocrine secretion and expand our knowledge of the signalling systems employed by this peptide.

1F32MH012142-01
BASHAM, MARK
TPA ACTIVITY AND CEREBELLAR MOTOR LEARNING
UNIVERSITY OF COLORADO HLTH SCIENCES CTR
DENVER, COLORADO

DESCRIPTION (adapted from applicant's abstract) : Although memories may be stored in a variety of ways, increasing evidence suggests that at least some memories are stored as changes in the strength of connections between neurons. Recently two types of memory that involve changes in synapse strength or number, long-term potentiation (LTP) and cerebellar motor learning, have been associate with an increase in mRNA for tissue-type plasminogen activator (tPA). This suggest that tPA activity may facilitate motor learning. However, such a role for tPA has not been confirmed. Therefore, our first experiments test whether blocking tPA activity or deleting the tPA gene impairs cerebellar motor learning. In addition, we will determine whether tPA facilitates motor learning through the conversion of plasminogen to plasmin, and also whether motor learning in tPA-/- mice involves persistent modulations of GABAergic activity.
Finally, the biochemical and molecular events that regulate tPA activity have not been identified. However, many examples of activity- dependent plasticity require activation of NMDA receptors and at least some of these are also associated with an increase in tPA mRNA. This suggest that NMDA receptors are involved in the regulation of tPA activity. Our final experiments will utilize pharmacological blockade of NMDA receptors to determine whether cerebellar motor learning requires activation of NMDA receptors and whether blocking those receptors during motor learning prevents the increase in tPA mRNA expression. Taken together these experiments will provide insight into tPA's role in memory formation and, more generally, into the mechanisms of activity-dependent plasticity.

1F31MH012102-01
BEARDEN, CARRIE
CLINICAL AND COGNITIVE PATTERNS IN CHILD SCHIZOPHRENIA
UNIVERSITY OF PENNSYLVANIA
PHILADELPHIA, PENNSYLVANIA

DESCRIPTION (Adapted from Applicant's Abstract) : There is an accumulating body of evidence that schizophrenia is a neurodevelopmental disorder (e.g., Weinberger, 1987). While the clinical expression of the illness is typically delayed for about 2 decades after birth, a small number of cases develop psychotic symptoms much earlier. Currently, the relationship between the child- and adult-onset forms of the disorder is poorly understood. This atypical early onset may represent a more severe variant of the illness. The proposed research will address the question of whether

early-onset schizophrenia is qualitatively and quantitatively similar to the adult onset form at the level of symptomatic presentation and cognitive function, by administering a comprehensive neuropsychological battery and clinical evaluation to a sample of 24 neuroleptic-naive, first-episode schizophrenics aged 8-16 and a demographically matched normal control group. A neuropsychological deficit profile that is qualitatively similar to adult-onset patients (i.e., selective deficits in attention, verbal learning and memory) would provide evidence of continuity between the child- and adult-onset forms. At the level of clinical symptoms, which reflect cognitive function in the broadest sense, this study will assess the prevalence and severity of specific positive and negative symptoms to determine whether the distribution of symptoms is similar to that of first-episode adult patients. As the first study of drug-naive patients in this age range, these findings will advance understanding of neurodevelopmental origins of the illness.

1F31MH012209-01
BEAUCHAINE, THEODORE
PSYCHOPHYSIOLOGY OF DISINHIBITION IN ADOLESCENTS
STATE UNIVERSITY NEW YORK STONY BROOK
STONY BROOK, NEW YORK

DESCRIPTION (Adapted from Applicant's Abstract) : The proposed research will examine differential patterns of electrodermal and cardiac reactivity among conduct-disordered (CD), attention deficit hyperactivity-disordered (ADHD), and control groups of adolescents. Research by Fowles (1980, 1988) and others suggests that electrodermal reactivity during extinction, and heart rate reactivity during reward, represent the functioning of Gray's (1982a, 1982b, 1987a, 1987b) behavioral inhibition (BIS and behavioral activation (BAS) systems, respectively. According to this model, the disinhibition characteristic of both CD and ADHD results from an underactive BIS, an overactive BAS, or both. While deficits in electrodermal reactivity have been demonstrated in both CD and ADHD samples, heart rate is a contaminated measure of the sympathetically-mediated BAS, because it is also determined by parasympathetic input. This is particularly problematic given recent reports of deficits in parasympathetic functioning in CD samples. In the proposed research, electrodermal activity and appropriate measures of both sympathetic (pre-ejection period) and parasympathetic (vagal tone) influences on cardiac functioning will be assessed during reward, extinction, and passive coping. The pattern of results yielded is expected to provide an increment in specificity over Gray's model, with ADHD group exhibiting deficits in sympathetic functioning, and the CD group exhibiting deficits in both sympathetic and parasympathetic functioning compared to controls. This pattern would suggest a modification of Gray's model toward accounting for the aggression that accompanies behavioral disinhibition on CD but not ADHD samples.

1F30MH012174-01
BEJAR, RAFAEL
CAM KINASE II AND LEARNING AND MEMORY
UNIVERSITY OF CALIFORNIA SAN DIEGO
SAND DIEGO, CALIFORNIA

DESCRIPTION (Adapted from applicant's abstract) : The long-term objective of this research is to provide a clearer understanding of the molecular basis

of synaptic plasticity and how this relates to learning, memory, and behavior. This is an important health-related issue because abnormal neuronal function has been implicated in the pathoetiology of several diseases including psychiatric disorders, ischemic brain injury, and Alzheimer's disease. This line of research is also relevant to age- related changes in memory function. We propose to study the mechanisms through which an overexpressed Ca2+-independent form of calmodulin-dependent kinase II (CaMKII-Asp286) disrupts both synaptic plasticity in the hippocampus and behavioral performance on spatial memory-dependent tasks. Our specific aims are (1) to determine whether calmodulin trapping by CaMKII-Asp286 is sufficient to produce the physiological and behavioral phenotype observed in mice expressing this Ca2+-independent form of CaMKII, (2) to determine if disruption of synaptic plasticity by CaMKII-Asp286 in the CA1 region of the hippocampus alone is sufficient to produce a deficit in spatial learning and memory, and (3) to identify which stage of learning and memory, either acquisition, consolidation, or recall, is sensitive to disruption by expression of the CaMKII-Asp286 transgene. These aims will be accomplished by studying the activity of CaMKII-Asp286 in vitro, by creating two new lines of transgenic mice, and by testing these and existing transgenic animals on spatial tasks. First, we plan to create a line of mice carrying a Ca2+-independent form of CaMKII that has no kinase activity in order to determine if calmodulin trapping alone can create a phenotype similar to that seen in our existing mice. Using the CRE-lox system, we will create a second line of mice which expresses the CaMKII-Asp286 only in the CA1 region of the hippocampus. Finally, the existing mice we plan to study suppress CaMKII-Asp286 expression in response to tetracycline. This will allow us to regulate at which time after learning the transgene is expressed and is capable of disrupting spatial memory.

1F31MH012113-01
BENJAMIN AMY
REPRODUCTIVE DECISION MAKING AMONG HIV INFECTED WOMEN
UNIVERSITY OF COLORADO AT DENVER
DENVER, COLORADO

DESCRIPTION (Adapted from Applicant's Abstract):
The growing HIV epidemic among women, parallel epidemic of pediatric AIDS, and increasing use of prenatal therapy to prevent vertical HIV transmission focuses critical attention on the outcomes of HIV-infected women's reproductive decisions. Yet the process and determinants of these reproductive decisions have been little studied or systematically evaluated. This study uses qualitative methods to a) develop an ethnographic profile of HIV-infected women's reproductive decision-making; and b) identify and link multiple levels of influence on their reproductive decisions. Specific Aims will generate in- depth understanding of HIV-infected women and 1) key individual and social factors that influence their reproductive decisions; 2) external conditions that impact their reproductive choices or ability to exercise those choices; and 3) the impact of existing policies intended to reduce vertical HIV transmission and of clinical advances (such as prenatal therapy) on their reproductive decisions. In-depth interviews are conducted with HIV-infected women and their care providers. Participant observation is conducted with a sub-sample of women chosen for case interest and theoretical relevance. Levels and pathways of influence on reproductive decisions are analyzed based on a Conditional Matrix. The synthesis of in-depth case study data and broad contextual understanding will generate grounded theoretical hypotheses to address

the specific aims. The results of this research will fill information gaps on HIV-infected women's reproductive decision-making, inform existing policies and interventions targeting HIV-infected women, and identify areas for further qualitative and quantitative research.

5F32MH011756-02
BERGMAN, ERIK
PRIMING ON IMPLICIT MEMORY TASKS
WASHINGTON UNIVERSITY

DESCRIPTION (Adapted from Applicant's Abstract):
Traditionally, learning and memory has been studied with tasks which direct individuals to explicitly recall or recognize events of the recent past in the last decade, psychologists have come to study memory through a set of measures that make no explicit reference to the past, and indirectly demonstrate transfer of past experience regardless of conscious awareness or intent. Such implicit measures behave differently from traditional explicit measures of memory; performance is often uncorrelated or dissociated on the two types of tests. Variables that affect explicit memory in one way often have no effect or opposite effects on implicit measures of memory.
One explanation for the differences between implicit and explicit measures of memory is that they rely on in dependent memory systems with distinct principles of operation. Alternately, the processing approach attempts to explain such differences using existing theories of memory. The proposed research will examine implicit memory phenomena, with particular focus on the processing approach. First , a series of experiments will examine a phenomenon which challenges processing theory. Next a new technique (unit analysis) will be used to examine in detail the precise pattern of differences between implicit and explicit memory, with particular focus on the predictions of both systems and processing theory. Finally, the possibility that processing theory can be extended to explain implicit memory for objects will be examined in several experiments.

1F31MH012287-01
BESTER-MEREDITH, JANET
VASOPRESSIN--A ROLE IN AGGRESSION AND PARENTAL CARE
UNIVERSITY OF WISCONSIN MADISON
MADISON, WISCONSIN

DESCRIPTION (applicant's abstract) : These studies will illustrate how the arginine vasopressin (AVP) neuropeptide system responds to changes in an animal's social environment. Within a specific pathway originating in the bed nucleus of the stria terminalis (BNST) and medial amygdala (MA), AVP has been associated with aggression and parental care. The studies described in this proposal are designed to examine the flexibility of this neurotransmitter system by examining whether: (1) aggression and parental care are affected by the social environment during development, (2) flexibility in social behavior is associated with changes in AVP and (3) AVP injections produce changes in aggression and/or parental care. In order to answer these questions, this stud will examine how species-typical patterns of social behavior can be altered by cross-fostering two species of mice that show different patterns of aggression and parental care. By examining the behavior of adult cross-fostered mice, thi study will show whether aggression and parental care are altered by changes in the social environment during development. A second goal of this study is to use

immunocytochemistry to examine whether changes in aggression and parental behavior are associated with changes in the pattern of AVP distribution within the brain. Finally, this project will examine how the context of a behavior ma modulate the effects of AVP by examining the effects of intracerebroventricula AVP injections under different contexts. Together , these studies will clarify the role of AVP in regulating species-typical patterns of aggressive and parental behavior and show how developmental influences can alter a specific neurotransmitter system.

5F30MH011349-03
BLAINE JUDITH
MOLECULAR IDENTIFICATION OF FUNCTIONAL K+ CHANNELS
UNIVERSITY OF COLORADO HLTH SCIENCES CTR
DENVER, COLORADO

DESCRIPTION (Adapted from Applicant's Abstract):
Xenopus laevis provides an ideal animal model for the study of the developing vertebrate nervous system as the developmental stages in this species have been extremely well characterized. In addition, the use of standard in vitro fertilization techniques allows the production of embryos of any age whose neurons can be examined for the acquisition of electrical excitability. Amphibian spinal neurons first demonstrate action potentials at the neural plate stage (22 hr after fertilization). These impulses are calcium-dependent and of long duration. During the following 24 hours, the form of the action potential changes markedly, becoming the brief, sodium-driven spike characteristic of mature neurons. Previous work has shown that the transition from the mature to the immature wave-form is primarily due to the maturation of a delayed rectifier potassium current. During this develop mental transition the calcium current changes little while the sodium current doubles in density. The potassium current, however, triples in density and also demonstrates faster kinetics. Mathematical reconstruction of action potentials has also shown that the change in the shape of the impulse can be accounted for by the alternation in potassium current properties. The molecular bases underlying these stereotyped changes remain, as yet, unknown. A goal of my project is to match the molecular identities of the potassium channels cloned thus far in Xenopus with the functional potassium channel populations recorded from developing amphibian spinal neurons. Transcripts from two of the four known alpha subunit genes in Xenopus, Kv1.1 (a member of the Shaker-like subfamily) and Kv2.2 (a member of the Shab like subfamily), have been shown by in situ hybridization and single-cell reverse transcriptase PCR to be present in the developing amphibian spinal cord. In addition, these channels induce delayed rectifier potassium currents when expressed in the Xenopus oocyte. Kv1.1 and Kv2.2 gene products are thus likely candidates for the induction of currents leading to the shortening and maturation of the action potential.
The work outlined above should allow the identification of endogenous functional single channels that contain Kvc1 and/or Kv2 subunits. This is significant as to date, no experiments have matched the molecular identity of gene with a functional channel population recorded from the developing spinal cord. The next step would be an elucidation of the mechanisms involved in the transcription of the gene of interest - i.e. a determination of why that particular gene is transcribed in a specific neuronal subset at a certain developmental stage. Ultimately such knowledge will provide a more complete understanding of the events involved in the acquisition of electrical excitability and hence the possibility of designing more effective therapies for the treatment of disorders of the

developing nervous system and those disorders due to improper due to improper excitation such as epilepsy.

1F31MH012018-01
BLOOM,ALEXANDRA
PREVENTING RECURRENT HOMELESSNESS IN THE MENTALLY ILL
ADELPHI UNIVERSITY
GARDEN CITY, NEW YORK

DESCRIPTION (Applicant's abstract) : The goal of the proposed study is to do a process-oriented program evaluation of the Critical Time Intervention (CTI) (Susser & Valencia, 1997), an innovative approach to prevent recurrent homelessness in a group of mentally ill men. CTI was designed to prevent homelessness by improving the continuity of care for individuals being discharged from institutional to community living. (CTI group=48, control group=48). CTI workers provided services based on both clinical judgment and clients' assessments of their service needs. While many interventions with this group fail because of disagreements between clients and service providers, CTI bridges this gap by allowing a collaborative alliance between the two. The results of this controlled study ;showed that CTI was effective in reducing homeless nights. However, although this major outcome assessment has been done, it is still not clear what about the program was effective with which clients under what circumstances. The specific aims of this study will be to examine several other process and outcome variab1es of the CTI intervention, such as range and frequency of services used by men in the CTI group, the type of housing CTI clients gravitated to, and their quality of life ratings as compared to men in the control group. Schizophrenic symptomatology and substance abuse will be examined as possible modifiers of CTI' S effect. This information will then be used to refine the design of CTI, in order to use it with mentally ill individuals discharged from a state hospital into the community.

5F31MH011884-02
BOADA, RICHARD
IMPLICIT PHONOLOGICAL REPRESENTATIONS IN DYSLEXIA
UNIVERSITY OF DENVER
AURORA, COLORADO

DESCRIPTION (Adapted from Applicant's Abstract):
The proposed research will test the segmentation hypothesis in young dyslexics by assessing the nature of their underlying phonological representation. In order to establish convergent validity, three tasks that are not confounded by metalinguistic, temporal or articulatory confounds will be used to measure implicit phonological representations. Dyslexic's performance on a syllable similarity task, a agate lexical retrieval task, and a priming task will be compared to chronological and reading age matched controls (n-25 in each group), in order to ascertain whether their underlying phonological development is delayed or deviant. The level of functioning on these measures of underlying phonological development will be related to performance on a labeling paradigm that evaluates developmental changes in the weights given to different acoustic cues in the perception of speech. In order to assess whether deficient phonological representations are a primary cause of dyslexia, the relationship and measures of phoneme awareness, reading ability and other associated features of dyslexia (rapid naming, short term verbal memory, and non-word repetition deficits) will be described. Understanding the nature of phonological development beneath the level of phoneme awareness is important

for the development of more effective intervention and prevention strategies for dyslexic individuals.

5F31MH011896-02
BOETTIGER, CHARLOTTE
DEVELOPMENTAL CHANGES IN THE CIRCUIT OF SONGBIRD NUCLEUS
UNIVERSITY OF CALIFORNIA SAN FRANCISCO
SAN FRANCISCO, CALIFORNIA

DESCRIPTION (Adapted from applicant's abstract) : The songbird nucleus LMAN appears to play an important role in song learning, perhaps by providing auditory feedback to the motor system via its projection neurons. During the course of song learning, the response properties of these neurons are dramatically modified by the bird's experience. The responses evolve from a state of broad responsiveness for complex auditory stimuli to a state of pronounced selectivity for the bird's own song. The development of this response selectiveness is hypothesized to be critical to normal motor learning of song production. The cellular and synaptic bases of these selective properties are unknown. A long term goal of the proposed work is to develop a detailed model of the cellular changes occurring in LMAN during development. Specifically, the proposed investigation will elucidate the functional organization of LMAN using two parallel approaches : in vitro acute slice electrophysiology and in vivo fluorescent double-labeling combined with confocal microscopy. Planned experiments will focus on the glutamatergic and GABAergic components of the circuitry. Developmental changes in glutamatergic transmission in LMAN will be assessed, particularly in terms of activity dependent long-term plasticity phenomena. In addition, LMAN projection neurons will be examined for developmental increases in GABAergic transmission.

5F31MH011519-03
BOLTON, MARTHA
NEUROTROPHIN REGULATION OF GLUTAMATE RECEPTORS IN CORTEX
DUKE UNIVERSITY
DURHAM, NORTH CAROLINA

DESCRIPTION (Adapted from Applicant's Abstract):
The overall goal of this project is to determine how neurotrophins regulate synaptic transmission in the developing neocortex. In the visual cortex, there is a change in the kinetics of NMDA mediated synaptic responses over the course of development beginning around the time of eye opening (Carmignoto and Vicini 1992). In neonates, the duration of synaptic responses is much longer than in the adult. In the somatosensory cortex (SI), a similar kinetic shift also occurs, but at a slightly earlier age, beginning at P7. Simultaneously, in the somatosensory cortex, the ratio of the peak evoked NMDA to AMPA currents is reduced 5-fold (Crair and Malenka 1995). In this study, I will test the hypothesis that neurotrophins are necessary and sufficient to induce these developmental changes in synaptic transmission. I will examine this question electrophysiologically, using whole cell patch-clamp. The preparation will be organotypic slice cultures which combine the preservation of circuitry of the acute slice with the ability to do extended experimental manipulations of dissociated cell culture. To determine if neurotrophins are sufficient to induce this synaptic maturation, I will apply exogenous neurotrophins and observe the kinetics of synaptic responses. To determine if they are necessary, I will prevent the actions of endogenous neurotrophins with receptor -bodies, chimeric

proteins composed of the extracellular domain of the neurotrophin trk receptor and an IgG heavy chain. If neurotrophins cause this developmental change in transmission, then antagonizing their action with receptor bodies should prevent it.

1F31MH012071-01A1
BONI, LEANN
NONVERBAL EMOTIONAL PROCESSING IN SICKLE CELL CHILDREN
EMORY UNIVERSITY
ATLANTA, GEORGIA

DESCRIPTION (Adapted from Applicant's Abstract) : The present investigation represents an initial step toward determining the etiological contributors to social-emotional deficits in children with sickle cell disease (SCD). Specifically, the relationship between neurologic insult and social-emotional processing in children with SCD will be examined. Understanding the pathophysiology of these deficits facilitates the development of behavioral interventions. Using MRI to document neurologic insult, this study will compare four groups of SCD children (right hemisphere damage, left hemisphere damage, bilateral damage, normal) on a well-normed and ecologically valid measure of receptive prosody and facial affect recognition (DANVA). The relationship between nonverbal processing abilities and other neurocognitive functions will be evaluated with measures of interpersonal (SSRS), emotional (CDI, CBCL), academic (WJ-R), and intellectual ability (WISC-III). Findings from SCD participants will be compared to non-SCD African American controls. Specific goals include : 1. To determine whether social-emotional deficits in SCD youth are related to impaired receptive nonverbal communication skills; 2. To determine the relationship between processing skills and interpersonal, emotional, and academic functioning; 3. To determine the relationship between processing skills and site of neurologic insult as determined by MRI scans.

5F30MH010890-05
BORDELON, YVETTE
DNA CLEAVAGE IN EXCITOTOXIC CELL DEATH IN STRIATUM
UNIVERSITY OF PENNSYLVANIA
PHILADELPHIA, PENNSYLVANIA

DESCRIPTION (Adapted from applicant’s abstract) : Excitotoxicity has been implicated as a contributor to several pathological states including hypoxia, hypoglycemia, and neurodegenerative diseases. The exact mechanisms leading to delayed neuronal death induced by excitotoxins are unknown. It has recently been shown in the sponsor’s laboratory that DNA cleavage detected by in situ nick translation occurs early in excitotoxic cell death and can be a useful index of cell damage. The outlined project plans to use this technique to examine the time course of DNA cleavage in striatal neurons in vivo and in vitro after exposure to quinolinic acid. A combined in situ hybridization and in situ nick translation approach will be used to determine whether differential vulnerability of striatal gamma aminobutyric acid (GABA)ergic neurons to excitotoxicity corresponds to the expression of the neuropeptides enkephalin or substance P. In addition, the plan will determine whether glutamate antagonists need to be administered prior to the appearance of DNA strand breaks to produce neuroprotection in vivo and in vitro. It is proposed that these results may provide new insights into the mechanisms involved in, and the factors affecting, excitotoxic cell death towards the broader objective of developing future experiments to explore the mechanisms involved

in neuronal death after ischemia or in degenerative disease, and in designing new therapeutic approaches to ameliorate these significant health problems.

5F31MH011404-03
BRAGDON, EDITH
CARDIOVASCULAR & PAIN TOLERANCE RESPONSES IN HEALTHY ADU
UNIVERSITY OF NORTH CAROLINA CHAPEL HILL
CHAPEL HILL, NORTH CAROLINA

DESCRIPTION (Adapted from Applicant's Abstract):
The proposed study will examine several issues pertaining to the effect of behavioral stress on cardiovascular and pain regulatory systems and their possible interaction in healthy men and women with depressed mood but without major depression or any chronic pain disorder. Measures of thermal and ischemic pain sensitivity will be assessed at baseline and after a 5-minute stress (stress day) or rest (control day) period. Systolic and diastolic blood pressure, heart rate., impedance-derived estimates of stroke volume, cardiac output, and total peripheral resistance, and beta-endorphin and catecholamine levels will be measured during baseline, rest and stress periods, and accompanying pain measurement. A major goal is to extend my previous findings relating stress-induced analgesia to blood pressure reactivity to stress in normotensive humans. The study's results may have implications for models of psychophysiological mechanisms contributing to the development of cardiovascular disease, and for the experience of anginal pain versus painless (silent) myocardial ischemia in patients with coronary heart disease.

1F31MH012065-01
BRANNON, ELIZABETH
ORDINAL AND CARDINAL NUMERICAL COMPETENCE OF MACAQUES
COLUMBIA UNIV NEW YORK MORNINGSIDE
NEW YORK, NEW YORK

DESCRIPTION (adapted from applicant's abstract) : The numerical competence of rhesus monkeys will be investigated to provide an animal model of the non-linguistic representation of number. The proposed research will focus on the ability of monkeys to determine the ordinal and cardinal values of novel exemplars of familiar and unfamiliar numerosities. Ordinal competence will be assessed in experiments in which monkeys are first trained on the numerosities 1-4 in a list learning paradigm. They will subsequently be tested on pair-wise judgements of exemplar of the trained numerosities 1-4 and of the untrained numerosities 5-9. No reinforcement will be provided during tests with the novel numerosities 5-9. That will provide a basis for determining if monkeys have an ordinal representation of numerosity. Cardinal competence will be studied in a second series of experiments with a variation of the widely used matching-to-sample paradigm. Subjects will be required to match the sample by selecting a physically distinct choice stimulus that contains the same number of elements as the sample, i.e., to match solely on the basis of cardinal number. Reaction time data will be analyzed to model how monkeys represent ordinal and cardinal numerosities, and to evaluate the hitherto unsubstantiated claim that subitizing accounts for all non-human numerical discriminations.

5F31MH011749-02
BRELSFORD, KRISTIN
EXECUTIVE IMPAIRMENT IN AUTISM, ADHD AND SCHIZOPHRENIA
UNIVERSITY OF DENVER

DENVER, COLORADO

DESCRIPTION (Adapted from Applicant's Abstract) : The proposed research will compare profiles of performance on executive function tasks in individuals with high-functioning autism (HFA), attention-deficit/hyperactivity disorder (ADHD), and schizophrenia, in order to help clarify the underlying cognitive deficit in each. In particular, two key dimensions of executive functions will be studies: working memory and inhibition. This study will directly compare profiles of executive function across these three populations at comparable ages and developmental levels. In addition, verbal working memory, nonverbal working memory, and inhibition will be examined within a single clinical sample, to directly compare different components of executive functions. It is predicted that, compared to matched controls without disabilities (n=20), adults with HFA (n=20) will have working memory impairments, wit verbal working memory showing greater impairments than nonverbal working memory, but inhibition will be intact. Adults with ADHD (n=20) will have intact working memory, but inhibition will be impaired, while adults with schizophrenia will show impairment in both working memory and inhibition. If profile differences are found, the result will provide further evidence that some aspects of executive function are specific to certain disorders.

1F32MH012203-01
BRODKIN, EDWARD
GENETIC ANALYSIS OF ANXIETY RELATED BEHAVIORS
YALE UNIVERSITY
NEW HAVEN, CONNECTICUT

DESCRIPTION (adapted from applicant's abstract) :Anxiety is prevalent, disabling, and costly. The identification of genes that predispose individuals to anxiety should greatly improve our ability to prevent, diagnose, and treat various psychiatric disorders. The goal of my proposed work during the NRSA Fellowship is to use quantitative trait locus analysis to identify loci (and, if possible, the genes within the loci) that affect-related behaviors in particular inbred mouse strains. Two inbred mouse strains that differ greatly in anxiety-related behaviors (as measured in the elevated plus-maze [EPM] and dark-light box [DLB] assays) will be identified. First- generation hybrid (F1) animals (produced by crossbreeding the two strains) will be backcrossed to one of the parental strains to produce a population of 250 to 400 second-generation (N2) animals. Each N2 generation animal will undergo the EPM and DLB assays of anxiety. Those N2 animals that show extreme (high or low) levels of anxiety-related behaviors will undergo genotyping using microsatellite markers. Quantitative trait loci (QTLs) will be localized by finding correlations between levels of behavior and the presence of particular microsatellite markers. The expressed sequence tag database will then be searched for genes in the region of the QTLs that might be candidates for anxiety-related traits. If there are no candidate genes located within the QTLs that prove to be associated with the anxiety-related behaviors, advanced intercross lines will be produced for fine genetic mapping of the QTLs. My hope is that this work will ultimately lead to the identification of homologous human genes that predispose people to severe anxiety.

5F31MH011219-03
BROMANN, PAUL
MOLECULAR BASIS FOR PROTEIN/PHOSPHOLIPID INTERACTION
NORTHWESTERN UNIVERSITY

CHICAGO, ILLINOIS

DESCRIPTION (Adapted from Applicant's Abstract):
This grant is requested to determine the molecular mechanisms of regulation of PLC delta1. The ability of proteins (such as G proteins), kinases, calcium fluxes, and lipids to regulate PLC delta1 activity will be assessed biochemically in vitro with purified components and biologically in vivo using transfeCted mammalian cells. Our work thus far has identified a regulatory domain in the N- terminal portion of a human PLC delta1 molecule. This region contains a recently identified 100 amino acid domain termed the pleckstrin-homology (PH) domain, which is present in many molecules involved in signal transduction. While several investigators have proposed that the PH domain is involved in mediating protein-protein interactions, our data instead suggest that this domain mediates lipid-protein interactions. We have demonstrated binding of several proteins containing PH domains (PLC delta1 and beta- adrenergic receptor kinase (beta-ARK)) to phospholipids with specificity and high affinity (mu M). Initial mutagenesis studies on PLC delta 1 have localized the phospholipid binding site to sub-domains 1 and 2 of the PH domain. We will test the hypothesis that PLC delta1 is primarily regulated by the translocation of the effector enzyme to its substrate phospholipid through the PH domain.

5F32MH011580-02
BROWN, EDSON
DO CORTICOSTEROIDS PROVIDE A MODEL FOR BIPOLAR DISORDER?
UNIVERSITY OF TEXAS SW MED CTR/DALLAS
DALLAS, TEXAS

DESCRIPTION (adapted from applicant's abstract) :The psychiatric side effects of exogenous corticosteroids, such as prednisone, have been described for over forty years, but not well characterized. The limited data available suggest that psychosis and mood symptoms are common, though risk factors are not known. The symptoms appear strikingly similar to those observed in bipolar disorder. This study will investigate the effects of standard medical boluses of corticosteroids in patients with asthma using structured clinical interviews and standard psychiatric rating scales. The effects of multiple courses and risk factors for developing symptoms will be explored. This investigation will provide valuable data on the frequency and nature of mood symptoms with corticosteroids, and will be the first to examine the effects of multiple courses. If the symptomatology does in fact closely parallel that seen in bipolar disorder, the effects of corticosteroids could provide the first satisfactory model for this severe illness.

1F32MH011767-01A1
BUDSON, ANDREW
DIAGNOSING DEMENTIA USING FALSE RECOGNITION
HARVARD UNIVERSITY
BOSTON, MASSCHUSETTS

DESCRIPTION (Adapted from Applicant's Abstract):
Patients with dementia often suffer from distortions of memory which impair their ability to live independently. This proposal will (1) investigate memory distortion in dementia patients by examining a) the susceptibility of patients with Alzheimer's disease (AD) and frontal

lobe dementia (FLD) to illusory memories, and b) the neuroanatomical correlates of this susceptibility to illusory memories. Additionally, as treatments for specific dementias emerge, the need for simple, non-invasive diagnostic tests becomes imperative. Thus, this proposal will also (2) determine the clinical utility of an illusory memory test to distinguish FLD from AD. Experiments 1-3 test the hypothesis that patients with FLD are more susceptible than controls to illusory memories in semantic, perceptual, and pictorial false recognition paradigms. Experiments 4-6 test the hypothesis that patients with AD are less susceptible than controls to illusory memories using these same false recognition paradigms. Experiment uses single photon emission tomography to test the hypothesis that susceptibility to illusory memories correlates positively with perfusion defects in prefrontal regions and negatively with defects in medial temporal lobe regions. Experiment 8 tests the hypothesis that, because of the double dissociation predicted from Experiments 1-6, false recognition tests will distinguish AD and FLD patients equally or better than other methods. Collectively, these studies will provide both a better understanding of illusory memories in dementia as well as a potential new method of diagnosing patients with AD and FLD.

5F31MH011747-02
BUSS, KRISTIN
PHYSIOLOGY OF TEMPERAMENT IN INFANTS AND CHILDREN
UNIVERSITY OF WISCONSIN MADISON
MADISON, WISCONSIN

DESCRIPTION (Adapted from applicant’s abstract) : Study of the relation between physiology and infant and early childhood temperament enhances understanding of individual differences in normative development will provide a framework for which to study developmental psychopathology. This project proposes the use of psychophysiological (electrocardiograph and impedance cardiography), neuroendocrine (salivary cortisol), extensive behavioral observation (laboratory temperament assessment), and parental report (temperament questionnaires) techniques to assess different aspects of temperament and emotional development in normally developing infants, toddlers, and preschoolers. This application involves three projects: an ongoing longitudinal laboratory twin study in infancy, an ongoing field study of over 400 preschoolers, and a newly designed laboratory study of toddlers. This multi-measure, multi-method project will provide replication and extension of research in the literature on the physiology of temperament. The specific relations between sympathetic and parasympathetic cardiac reactivity, and neuroendocrine reactivity in the context of the developing temperament have largely gone unstudied in the developmental literature until recent years. The ability to investigate these relations using a behavioral genetic twin design and large field study adds to the strength of this project.

1F32MH012145-01
CALTON, JEFFREY
POSTERIOR PARIETAL CORTEX AND INTENTION
WASHINGTON UNIVERSITY
ST. LOUIS, MISSOURI

DESCRIPTION (Adapted from applicant's abstract) : This investigation will utilize in vivo recordings in awake and behaving monkeys to address important questions regarding the role of the posterior parietal cortex in the decision to make movements to visual stimuli. A recent investigation

has demonstrated that some cells in this brain area are active when a goal directed eye movement is being planned to a visual stimulus, while other cells are active when a goal directed hand movement is being planned (Synder et al., 1997). This suggests that parietal cortex is actively involved in the decision to make one type of movement or another. However, in this previous study, the decision of movement type and movement location (what to do and where to do it) were made simultaneously, precluding separate analyses of the effect of these two different decisions on cell activity. In the current experiment, by separating these two decisions, it will be possible to determine if the activity of the posterior parietal cortex reflects the intention to make a particular type of movement before the spatial goal of that movement is available. The answer to this question will have important implications for the role of the posterior parietal cortex in decision making and for the process by which decisions are implemented in the brain.

5F31MH011866-02
CAMPBELL, HOLLY
NEURAL BASIS OF FORM PERCEPTION IN A MODEL VISUAL SYSTEM
UNIVERSITY OF ARIZONA
TUCSON, ARIZONA

DESCRIPTION (Adapted from applicant's abstract) :This proposal investigates the neural basis of orientation and form perception by a non-vertebrate model system, the dipteran Phaenicia sericata. The research will identify visual parameters pertinent to low-level form vision using behavioral tests. It will then employ these parameters as stimuli for testing the filter properties of identified neurons in a neuropil having neuroanatomical characteristics analogous to mammalian visual cortex. To understand mechanisms of visual perception, investigations at the single cell level must be performed against a background of detailed morphological analysis such that the structure of single neurons responding to specific visual stimuli can be related to the overall neuroanatomical context of the system. The dipteran compound eye and optic lobes offer an ideal substrate for such an investigation. The optic lobes' succession of retinotopically organized neuropils is functionally analogous to organization amongst mammalian visual regions, but contains orders of magnitude fewer neurons. In particular, the planned research will focus on the lobula, a neuropil supplied by the parvicellular element of this visual system and containing within it nerve cells that are structurally analogous to pyramidal and stellate neurons of mammalian cortex. The relative simplicity of this model system facilitates the identification of single computational units and allows detailed circuit analysis A further advantage of this simple system is that it reflects evolutionarily conserved principles of visual system design that cut across phylogenetic boundaries. The proposed will investigate : . the ability of a dipteran species to discriminate visual patterns and shapes containing orientation and texture information. . the cellular properties of neurons and circuits in the lobula that discriminate orientations and textures. . the anatomical organization of pyramidal-like and stellate-like neurons in the dipteran lobula.

5F32MH011402-03
CANLI, TURHAN
FUNCTIONAL MAGNETIC RESONANCE OF EMOTION
STANFORD UNIVERSITY
STANFORD, CALIFORNIA

DESCRIPTION (Adapted from Applicant's Abstract):

Two very different models of hemispheric specialization provide the starting point for this theory-driven research approach to examine the laterality of emotional learning and memory. The first is known as the valence hypothesis. It accounts for a number of observations on lateralized emotion processing, but was not designed to address issues of encoding and retrieval of affective information. The second is the HERA model, which was developed to account for a variety of findings on encoding and retrieval processes, but does not consider the affective content of the processed information. The work proposed here uses functional magnetic resonance imaging (fMRI) to test differing predictions made by these models about structures involved in the encoding and retrieval of affective information and has these two specific aims. Aim 1 : To determine whether specific brain structures are laterally activated by the encoding or retrieval of affective stimuli. A set of three experiments is proposed in which subjects encode affective stimuli designed to elicit broadly negative or positive affect, or the basic emotions of happiness or disgust (Exp. 1 a/b), engage in an emotional encoding and retrieval task (Exp. 2 a/b), and use imagery and recall of previously viewed films to experience emotions of happiness or disgust (Exp. 3). Aim 2: To determine whether specific brain structures are laterally activated by affective judgment based on the retrieval of neutral stimuli (the 'mere exposure' effect). The 'mere exposure' effect refers to the phenomenon that subjects prefer stimuli to which they have been previously exposed, irrespective of their awareness for the exposure. This observation led to a debate between Zajonc and Lazarus about whether higher cognitive (i.e., cortical) processing is necessary for affective judgment. A direct test is proposed , in which fMRI is used to identify cortical and subcortical systems that are activated in the mere exposure paradigm.

5F31MH011368-03
CARR, DAVID
DOPAMINE ACTIONS ON HIPPOCAMPO-PREFRONTAL TRANSMISSION
UNIVERSITY OF PITTSBURGH AT PITTSBURGH
PITTSBURGH, PENNSYLVANIA

DESCRIPTION (Adapted from Applicant's Abstract):
The hippocampal formation and prefrontal cortex (PFC) have both been demonstrated to participate in working memory processes, and the hippocampo-prefrontal pathway has been suggested to play an important developmental role in the pathology of schizophrenia. Dopamine (DA) afferents from the ventral tegmental area (VTA) have also been implicated in the learning and memory functions of the hippocampus and the PFC, and dysfunction of ascending DA projections has been suggested to be involved in the neuropathology of schizophrenia. It is not known, however, whether DA afferents are able to modulate hippocampo-prefrontal transmission. The proposed research will utilize in vivo neurophysiological methods in rats to examine the ability of DA, applied locally or released by VTA stimulation. to act on this pathway both at the cell body level and in the terminal field. In Study 1, the actions of DA will be recorded on hippocampal neurons identified as projecting to the PFC. In Study 2, the ability of DA to modulate the response of PFC neurons to hippocampal stimulation will be examined. In Study 3, the ability of DA to act presynaptically on hippocampal terminals will be examined by recording the terminal excitability of hippocampal afferents to the PFC. The mechanisms of DA action that are identified in these studies will improve the understanding of its role in cognitive and affective functions, as

well as its potential contribution to the pathophysiology and treatment of psychiatric and neurological disorders.

5F31MH011292-03
CARTER, CHRISTY
NEUROBIOLOGY OF COGNITIVE DEVELOPMENT--LATENT INHIBITION
UNIVERSITY OF NORTH CAROLINA CHAPEL HILL
CHAPEL HILL, NORTH CAROLINA

DESCRIPTION (Adapted from Applicant's Abstract):
This proposal is designed to examine the biological bases of a developmental change in latent inhibition (LI) of the classically conditioned eyelid response. Previous data from our lab suggests that conditioning emerges gradually between postnatal day 17 (PND17) and PND24 (Stanton, Freeman, & Skelton, 1992; Freeman, Spencer, Skelton, & Stanton, 1993). Recent work in infants in our lab makes it possible to look at not only the behavioral and the neurological development of eyelid conditioning in the rat which is known to be dependent on the cerebellum but to further extend this analysis to other brain structures, such as the hippocampus, and what their role might be in the modulation of higher order forms of learning, such as (LI), within this late developing learning system. In order to address these issues preliminary studies of LI have been carried out in our lab to begin to establish the ontogeny of this behavior. We have shown that while 20-day-old pups do not show latent inhibition, 24-and 32-day-old rats do. We propose to perform selective medial septal lesions and afterwards test pups on LI to see if this behavior is disrupted. The ontogeny of this behavior may reflect a developmental interaction between the hippocampus and cerebellum.

5F31MH011890-02
CARTER, JOHN
TANGSHAN EARTHQUAKE--STRESS AND ADOLESCENT SCHIZOTYPY
UNIVERSITY OF SOUTHERN CALIFORNIA
LOS ANGELES, CALIFORNIA

DESCRIPTION (Adapted from Applicant's Abstract):
606 Chinese 18-year-olds who experienced the Tangshan earthquake in utero were tested to determine incidence of psychological neuroanatomical dysfunction related to gestational period at which extreme stress was experienced. Measures obtained include the Schizotypal Personality Questionnaire, Raven's Progressive matrices, Hamilton Depression and anxiety Scales, and a CT brain scan. Those experiencing the earthquake during the second trimester of gestation, specifically the sixth month, are hypothesized to have a greater incidence of shizotypal syndromes. 606 Chinese 18-year-olds were tested on the same measures. This second group was matched to the first as to month of birth, but were born one year after the first group, and served as a control group. Severe stress may mimic a genetic error responsible for schizotypal features by disrupting the migration of vulnerable fetal neurons. Finds that support this theory may help to pinpoint the brain structures involved, and may suggest important prenatal preventative interventions. The proposal is for entry and verification of the data, detailed statistical analyses, and reports of all significant findings.

1F31MH012087-01
CHA, ALBERT
ION CHANNEL STRUCTURE AND FLUORESCENCE ENERGY TRANSFFER

UNIVERSITY OF CALIFORNIA LOS ANGELES
LOS ANGELES, CALIFORNIA

DESCRIPTION (Adapted from applicant's abstract) : Examining the relationship between structure and function in voltage-gated ion channels will not only clarify the fundamental mechanisms of cellular excitability, but will also explain how ion channels can malfunction. Ion channel mutations have been linked to disorders ranging from metabolic disturbances to heart arrhythmias, with possible links to epilepsy and other neurological disorders. Understanding the molecular mechanisms of voltage sensitivity in ion channels will not only lead to a better understanding of the electrical communication between neurons, but will also help explain the clinical manifestations of ion channel disorders. Current knowledge of voltage- gated ion channels indicates that different regions of the channel undergo conformational changes with voltage. However, the magnitude of these changes and their effects on channel structure are unknown, as is the tertiary structure of the protein. Measuring distances between different regions of the channel as a function of voltage will help elucidate the conformational changes associated with voltage gating. Fluorescence resonance energy transfer (FRET) has been used to measure the distance between two different fluorescent probes, a donor molecule and an acceptor molecule, by measuring the transfer of energy between the probes. By attaching one probe to a putative voltage-sensing region and the other to a static region of the channel, FRET has the potential to determine which regions of the channel move in response to voltage and the distances traveled by these regions from the closed to the open state of the channel.

1F31MH012017-01
CHHABILDAS, NOMITA
EXTERNAL VALIDITY OF THE DSM IV SUBTYPES OF ADHD
UNIVERSITY OF DENVER
DENVER, COLORADO

DESCRIPTION (Adapted from Applicant's Abstract) : The overall goal of the proposed research is to examine the external validity of the DSM-IV subtypes of Attention Deficit Hyperactivity Disorder, which include primarily inattentive (IA), hyperactive/impulsive (HI) and combined (COM) subtypes. Profiles of psychiatric comorbidity and performance on executive function (EF) tasks will be compared among the groups. There is some evidence of differential psychiatric disorders among the groups, but more work needs to be done in this area. It is predicted that the subtypes will have differential psychiatric correlates, with the IA subtype correlating more highly with internalizing disorders and the HI and COM groups correlating more highly with externalizing disorders. Further, very little work has been done on the neuropsychological profiles of the DSM-IV subtypes. It is predicted that the neuropsychological tests that tap inhibition will be differentially impaired in the groups, with only the HI and COM subtypes showing impairment on the variables directly relating to ability to inhibit, such as the commission errors on the Gordon and percent of inhibition and Stop Signal Reaction Time (SSRT) on the Stop Task. Evidence of differential psychiatric profiles and neuropsychological profiles would lend support for the external validity of the DSM-IV subtypes.

5F30MH010770-03
CHIEN, ANDY
SUBUNIT INTERACTIONS IN L-TYPE CALCIUM CHANNELS
NORTHWESTERN UNIVERSITY

EVANSTON, ILLINOIS

DESCRIPTION (Adapted from Applicant's Abstract):
L-type voltage activated calcium (Ca) channels are heteromultimeric proteins composed of a pore-forming alpha1 subunit and accessory subunits known as Beta, alpha2, delta, and gamma. Though electrophysiological studies have demonstrated that these accessory subunits are critical determinants of channel properties, the biochemical and molecular events underlying the interaction of these subunits is largely unknown. The proposed studies will address the hypothesis that multiple interactions are involved in the modulation of channel properties by accessory subunits. The two-hybrid system will be used to identify domains involved in protein-protein interactions. Subsequently, the functional significance of these interactions will be assessed in a mammalian cell expression system where a variety of immunological, pharmacological, and electrophysiological approaches can be used to evaluate channel properties and channel function. This multidisciplinary approach will lend further understanding into the mechanisms underlying Ca channel subunit associations, and consequently, channel function. Clinically, the elucidation of interacting domain will aid searches to identify novel pharmacological targets whereby Ca channels may be therapeutically manipulated, which would be extremely beneficial given the wide spectrum of disorders, particularly in the CNS, which are associated with changes in Ca homeostasis.

1F31MH012034-01
CHUKOSKIE, LEANNE
NEURAL REPRESENTATIONS OF MOTION DURING EYE MOVEMENTS
NEW YORK UNIVERSITY
NEW YORK, NEW YORK

DESCRIPTION (Adapted from applicant's abstract) : Movements of the eyes shift the retinal image by an amount equal to and opposite from that of the eye movement. The visual system must separate real world motion from retinal image shifts caused by eye movements so that motion of objects in the real world can be analyzed. The question is how and how well the neurons in the visual motion pathway can represent real world motion during movements of the eyes. Neurons in extrastriate area MT and the medial superior temporal area (MST) are selective for image direction and speed. In addition, some cells in area MST carry signals related to movements of the eyes. The experiments have two main goals : 1) to assess basic visual and smooth pursuit eye movement-related properties of MT and MST cells in awake, behaving monkeys; 2) to assess the degree to which visual and oculomotor signals interact in these same neurons. We will investigate these putative interactions by comparing responses to particular patterns of retina motion as monkeys both fixate and make smooth pursuit eye movements. Comparing speed and direction tuning under these viewing conditions will reveal the degree to which the responses of MT and MST cells compensate for movements of the eyes and represent motion of objects in the world.

1F31MH012118-01
CHURCHILL, JAMES
NEUROCHEMISTRY OF INJURY-INDUCED CORTICAL PLASTICITY
INDIANA UNIVERSITY BLOOMINGTON
BLOOMINGTON, INDIANA

DESCRIPTION (Adapted from applicant's abstract) : Within the past two decades, our meager understanding of how the adult brain can change has grown exponentially. The accessibility of somotosensory cortical areas and the highly reliable central representation of the body surface have provided a particularly fertile model by which to study adult neural plasticity. Manipulations of afferent stimulation patterns are accompanied by (now) predictable alterations in the topographic representation of the dermal surface. It is likely that many of the mechanisms by which somatosensory areas "learn" new responses after nerve injury are evolutionarily conserved in other brain areas as well. These changes can be beneficial or detrimental in nature and may manifest themselves as the ability to consolidate memory, or in the progression of a pathological disease. While injury induced reorganization in the somatosensory cortex has been extensively studied the mechanisms responsible for cortical plasticity have not been fully elucidated. In the present application, it is proposed that the neurochemical changes that occur during cortical reorganization be monitored and then compared to any neurochemical changes that might occur in response to deprivation alone. Such a subtractive analysis permits the identification of the neurochemical changes that are causal and those that are epiphenomenal.

5F30MH011582-03
CHYUNG, ABRAHAM
ALZHEIMERS DISEASE--APP PROCESSING IN NT2N NEURONS
UNIVERSITY OF PENNSYLVANIA
PHILADELPHIA, PENNSYLVANIA

DESCRIPTION (Adapted from applicant’s abstract) : Alzheimer’s disease (AD) is a major neurological disease of aging. Its prevalence is expected to increase well into the next century, but there still are no effective therapies. Theamyloid beta (AB) peptide deposited as insoluble amyloid in plaques and vascular deposits is one of the most striking neuropathological features of the AD brain, and these plaques may play a critical role in the pathogenesis of AD. The aim of this proposal is to examine the cellular processes that generate AB utilizing an in vitro system that closely models the neuronal cells of the human central nervous system. The ultimate goal of this project is to map the biochemical steps that mediate amyloid precursor protein (APP)processing to AB. To this end, the Semliki Forest Virus (SFV) vector system will be used to infect NT2N neurons with aberrant APP constructs bearing mutations in its cellular trafficking signal, the NPTY domain in thecytoplasmic tail. By utilizing missense mutations (NPTF and NPTC), deletion of the cytoplasmic tail, and replacement of the NPTY domain with the targeting signal from the lysosome-associated membrane protein-1 (Lamp-1), it will be possible to dissect the intracellular processing pathways. In other words, it will be possible to discern the cleavage steps that occur en route to the membrane, at the cell surface, and in the lysosomes. This will elucidate the mechanism(s) of AB production and provide clues to therapeutic strategies for its inhibition.

1F32MH012154-01
CIARAMITARO, VIVIAN
PARIETAL CORTEX, SPATIAL ATTENTION
NEW YORK UNIVERSITY
NEW YORK, NEW YORK

DESCRIPTION (Adapted from applicant's abstract) : This proposal outlines a comprehensive examination of the role of the lateral intra-parietal area (LIP) of parietal cortex in spatial attention. Clinical evidence implicates the parietal cortex in spatial attention; however, neurophysiological studies have not provided clear evidence for the role of parietal in attention. The majority of neurophysiological studies investigating attention provide no behavioral measure of attentional state. In the study proposed, attention is explicitly defined as the ability of an organism to alter visual processing efficiency at select spatial locations. A psychophysical methodology is presented, which enables us to re-direct attention to select spatial locations, and quantify attentional demand at a particular spatial location. Given that we can quantify an explicitly defined mental state, spatial attention, we will be able to determine to what extent changes in attentional state can be accounted for by underlying changes in the activity of neurons in area LIP. This research will be able to illuminate the role of area LIP in spatial attention and provide a framework for studies of attention in other brain areas.

5F31MH011717-02
CIBULSKY, SUSAN
CA++ CHANNEL BETA SUBUNITS IN CA++ CHANNEL MODULATION
UNIVERSITY OF COLORADO HLTH SCIENCES CTR
DENVER, COLORADO

DESCRIPTION (Adapted from Applicant's Abstract):
Neurotransmitter modulation of voltae-gated Ca2+ channel activity leads to the regulation of cellular processes such as neurotransmitter release, processing of electrical information in dendrites and gene expression. In CNS neurons, neither the biophysical nor the biochemical mechanisms of modulation are completely understood. The model system employed in the proposed research is comprised of somatostatin receptor type 4 (SSTR4) coexpressed with the pore-forming alpha and the auxiliary alpha 2 and beta subunits of Ca2+ channels in Xenopus oocytes. This sytem serves as a tool for reconstituting a modulatory pathway which allows me to study channel biophysics as well as structure-function relationships. We have previously demonstrated in this system that bath application of 1 upsilonM somatostatin (SST) inhibited peak Ba 2+ current; the magnitude of inhibition in cells expressing alpha1A, alpha2 but no beta was approximately three times that in cells expressing alpha1A, alpha2 and beta. This research plan is designed to determine the role of the Ca2+ channel beta subunit in the modulation of Ca2+ channel current by (1) determining the biophysical mechanism of modualtion and (2) identifying the structural elements of channel subunits required for modulation. The results of this research are anticipated to help answer the question: what is a modulated Ca2+ channel? Since voltage-gated Ca2+ channels are essential components in the processes of neurotransmitter release and information processing in dendrites, the mechanisms of their regulation are relevant to diseases of the central nervous system such as epilepsy.

1F31MH012039-01
COLLIVER, THOMAS
AMPEROMETRIC DETECTION AT SNAP 25 DEPLETED CELLS
PENNSYLVANIA STATE UNIVERSITY-UNIV PARK
UNIVERSITY PARK, PENNSYLVANIA

DESCRIPTION (adapted from applicant's abstract) : The mouse mutant coloboma mutation has been defined as a deletion mutation encompassing several genes on chromosome two, the hyperactivity of these mice has been shown to result directly from the depletion of SNAP-25. This protein is associated with the plasma membrane of presynaptic terminals and plays a critical role in neurotransmitter release. In coloboma mice, it is therefore, reasonable to conclude that decreased levels of SNAP-25 gives rise to abnormalities in presynaptic function that ultimately leads tot heir hyperactivity. Central to understanding the role of SNAP-25 in coloboma hyperactivity is defining, on the single-cell level, the changes in neurotransmitter release that result from decreased levels of this protein. The overall goal of this proposal is to use electrochemical methods to define how decreased levels of SNAP-25 can alter the release and storage of neurotransmitters at the single-cell level. Ultimately, these experiments should allow us to better understand how the cellular changes that result from decreased levels of a single protein, SNAP-25, lead to the hyperactivity of coloboma mice.

5F31MH011434-03
CONTOS, JAMES
TARGET GENE IDENTIFICATION OF EMX TRANSCRIPTION FACTORS
UNIVERSITY OF CALIFORNIA SAN DIEGO
LA JOLLA, CALIFORNIA

The long term objectives of the research proposed is to understand the molecular and cellular basis for the development of the cerebral cortex. The specific hypothesis we aim to investigate is that the embryonic cerebral cortex-restricted transcription factors Emx1 and/or Emx2 regulate the transcription of target genes with limits of expression demarcating the developing cerebral cortex. The approach taken is to determine endogenous expression levels of Emx1 and Emx2 in various murine neural cell lines, including several derived from the cortex, using Northern blots. Choosing a cell line with little endogenous Emx expression, an inducible Emx1 and/or Emx2 gene will be stably integrated using a calcium phosphate transfection protocol. The Emx genes will be highly expressed after removal of low levels of tetracycline from the cell culture medium. mRNA transcripts that are up- or downregulated after Einx induction will be identified using RDA and PCR differential display. Subtraction products will be screened for embryonic cerebral cortex expression using in situ hybridization, and the most interesting of these will be characterized by DNA sequencing. Understanding the molecular interactions responsible for normal development of the cerebral cortex could shed light on the multitude of characterized problems with this organ, ranging from dyslexia to schizophrenia.

1F31MH011998-01A1
COOPER, BRENTON
RETROSPLENIAL CORTEX CONTRIBUTIONS TO SPATIAL NAVIGATION
UNIVERSITY OF UTAH
SALT LAKE CITY, UTAH

DESCRIPTION (Adapted from applicant's abstract) : The present proposal seeks to address how multiple structures interact to mediate active navigation. The ability to learn and remember locations of important resources is absolutely critical for every animal's ability to survive. As such, it is of great importance to understand how neural systems interact to mediate this behavior. The proposed studies will evaluate cortical contributions to

processing of spatial information in hippocampus and limbic thalamus. Past anatomical, lesion and electrophysiological data suggest the retrosplenial cortex may make unique contributions to spatial learning. It is hypothesized here that retrosplenial cortex importantly contributes to the integration of visual and self movement information in limbic structures thought to be involved in navigation. To test this hypothesis, permanent lesions and temporary inactivation of retrosplenial cortex will be combined with chronic single unit recording from hippocampus and thalamus during active navigation. Behavioral probe trials will be used to identify changes in behavioral strategies following removal of retrosplenial cortex. It is predicted that in the absence of retrosplenial cortex the integration of visual and self movement information will be diminished in spatial correlates recorded from thalamus and hippocampus and behavioral data will reflect similar changes in behavioral strategies underlying spatial memory performance.

5F31MH011497-02
CORDOVA, ALLAN
CONFLICT MANAGEMENT AND TRIADIC FAMILY INTERACTION
UNIVERSITY OF DENVER
DENVER, COLORADO

DESCRIPTION (Adapted from applicant’s abstract) : Longitudinal and crosssectional data will be used to answer basic questions about child-absent and child-present marital communication and management of negative affect in the family, and the stability of these interactional processes. To achieve this goal, it will be necessary to construct and validate a microanalyticobservational coding system for use with a mother, father, and child participating in a laboratory discussion task. Observational and self-report data will be examined to test hypotheses regarding the extent to which marital conflict and negativity “spill over” into parent-child interactions, and conversely, the extent to which marital conflict is “encapsulated” and constructively managed in the presence of children. These hypotheses will be explored with 24 couples from an ongoing longitudinal sample and 36 cross-sectional, and their children (range = 4-7 ½ years old) who participated in a family interaction study. Development of a triadic microanalytic coding system would represent a significant methodological gain for the field of family interaction research, as most available observational coding systems are only suited for use with family dyads. In addition, results of this investigation may have important implications for programs focusing on prevention of family discord and childhood problems.

1F31MH012311-01
CORSICA, JOYCE
CARBOHYDRATE SELF ADMINISTRATION, MOOD, AND COGNITION
FINCH UNIV OF HLTH SCI/CHICAGO MED SCH
CHICAGO, ILLINOIS

DESCRIPTION (Applicant's Abstract) : This proposal is designed to investigate whether the phenomenon of carbohydrate craving can be objectively demonstrated and whether carbohydrate self-administration serves to self-medicate unwanted negative moods. The purpose of the study is to determine whether the effects of carbohydrates on mood and cognition that are reported by carbohydrate- cravers persist in a double-blind controlled study. It is predicted that the carbohydrate- craver will experience an improvement in both mood and cognition following ingestion of a carbohydrate-rich beverage versus a taste-matched protein-rich beverage,

even when expectations are controlled by blinding subjects to the micronutrient content of the beverage and that mood elevation will be greatest when carbohydrate is chosen and administered by the subject rather than by the experimenter. Mood is not expected to parallel blood glucose changes, excluding an explanatory mechanism based on hypo- or hyperglycemia. Results of this study will provide further insight into mechanisms that elevate carbohydrate-craving and consumption of carbohydrates and enhance our general understanding of how eating affects psychological well-being. This study may have implications for the treatment of eating disorders and depressive syndromes that are characterized by carbohydrate craving and over-consumption.

5F31MH011894-02
COTE, KIMBERLY
INFORMATION PROCESSING DURING SLEEP PHASIC EVENTS
UNIVERSITY OF OTTAWA
OTTAWA, CANADA

DESCRIPTION (Adapted from applicant's abstract) : The thesis will consist of a series of five studies which aim to investigate the functional role of phasic events in sleep. K-complexes and spindles are phasic events occurring in sleep whose role may be examined using neurophysiological methods such as averaged event-related potentials (ERPs), power spectral analysis, and voltage distribution brian mapping. Two studies have been completed thus far. The first study established the ERP as a reliable measure of the extent of information processing during sleep. More specifically, decreased negativity in the ERP parallelled lengthened reaction times (RTs) associated with the loss of consciousness at sleep onset. The second study demonstrated an inhibitory role for sleep spindles, by measuring the effects of high intensity auditory stimuli on information processing during spindle activity. Next, the applicant is proposing to further investigate the nature of this finding, by quantifying the temporal and topographic characteristics of the inhibition associated with sleep spindles. The fourth study will investigate the functional role of the K-complex in information processing during sleep, in order to determine whether it exists to protect sleep from disturbance or to alert the sleeper to the environment. Lastly, subsequent analysis of data collected in the preceding studies will investigate the occurrence of K-spindle activity, the phenomena where these phasic event occur together. These studies will elucidate the functional role of phasic events in sleep and thereby lead to a further understanding of normal sleep processes and various sleep pathologies.

1F31MH011987-01A1
COUNTS, SCOTT
TOPOLOGY AND SUBCELLULAR LOBALIZATION OF PRESENILIN-1
EMORY UNIVERSITY
ATLANTA, GEORGIA

DESCRIPTION (Adapted from applicant's abstract) : Mutations in the gene encoding presenilin-1 (PS1) protein are causative in the majority of early-onset familial Alzheimer's disease (FAD). Thus, a central focus of Alzheimer's research is to resolve the physiological role of PS1 in normal and PS1-linked FAD brain. Recent studies show that PS1 is a transmembrane protein confined to intracellular membrane compartments, where it undergoes endoproteolytic cleavage into N- and C-terminal fragments. The principal goal of this research is to utilize the specificity of monoclonal antibodies

recognizing N- and C-terminal domains of PS1 and a receptor epitope fused to serial truncations of PS1 to address two fundamental aspects of PS1 biology. First, an epitope protection assay and complementary immunogold-EM study will be adapted to determine the transmembrane topology of wild type PS1. Secondly, immunogold-EM will be employed to define the precise ultrastructural localization of processed PS1 derivatives. Taken together , these studies will be critical to understanding the subcellular interactions of PS1 with other molecules along the functional pathways of PS1 and along the structure of the protein itself. We will also examine the effects of select PS1 mutations on wild type topology and native N- and C-terminal fragment distribution to explore potential sources of mutant PS1 malfunction.

1F31MH012072-01A1
CRAWFORD, LAURA
EXPECTATION BIASES IN PERCEPTION OF COVARIATION
UNIVERSITY OF CHICAGO
CHICAGO, ILLINOIS

DESCRIPTION (Applicant's abstract) : The proposed study investigates the interaction between experience and expectation in correlation perception. The study uses implicit and explicit measures to explore monthly how people assess correlation, but also how people use actual feature correlations and expectations about correlations to make predictions and to be able to determin if prior expectations produce biases in representations of information, or if they produce response biases.

1F32MH012014-01A1
DAVIS, JAMES TIMOTHY
RISK AND RESILIENCE ACROSS THE LIFE COURSE
BRIGHAM & WOMEN'S HOSPITAL
BOSTON, MASSACHUSETTS

DESCRIPTION (Adapted from applicant's abstract) : The purpose of this research is to trace the natural history of risk and resilience across the life course through studying trajectories and turning points in resilience across the life course (Aim 1). Understanding how resilient individuals overcome serious adversity has considerable potential to inform the prevention and treatment of maladaptation in others who are similarly at risk. Although an extensively studied area in child development, virtually no research on resilience has been conducted which introduces this important construct into the middle and late phases of life. To examine resilience across the life course, the proposed research program will study a sample of 50 at-risk individuals who have been followed longitudinally for over 50 years (Glueck & Glueck, 1950; Vaillant, 1995). These 50 individuals have been interviewed at four points across the life course (ages 14, 25, 32, 47). They will be re-interviewed at a fifth point (age 67) for this research. Subjects will be considered to be 'resilient' at each point in the life course based on a global assessment of their psychological, social, and occupational functioning. A second aim will be to investigate Adult Attachment Status, Defense Mechanisms, and Ego Development as possible underlying mechanisms of resilience. A third aim will be to identify the life course antecedents of these proposed mechanisms.

5F31MH011228-02
DAY, ELAINE
MEDIAL CORTEX FUNCTION AND FORAGING STRATEGY IN LIZARDS

UNIVERSITY OF TEXAS
AUSTIN, TEXAS

DESCRIPTION (Adapted from Applicant's Abstract):
The mammalian and avian hippocampus appears to grow in response to natural selection pressures for spatial cognition. The proposed research will investigate if the structural homolog to the hippocampus in lizards, the medial cortex, is necessary for place memory and grows in response to the ecological demands of active foraging. The performance of Cnemidophorous inornatus males with lesions of the medial cortex and dorsal cortex will be compared to sham operated animals. I will examine two pairs of congeneric species of lacertids that have different foraging styles. It is expected that the active foragers will have better place memory and a larger medial cortex volume than sit-and-wait predators.
The study of the role of the medial cortex as a homologue to the hippocampus may provide more models for the analysis of memory and learning that may be useful for research relating to disorders involving hippocampal dysfunction including Alzheimer's, strokes, and accident-induced brain trauma. The molecular basis of memory via studies of long-term potentiation may also be studied using reptiles once we have a better understanding of the neural structures of learning and memory in this phyla.

1F32MH012159-01
DIMITROV, ALEXANDER
INFORMATION THEORETIC ANALYSIS OF NEURAL CODES
MONTANA STATE UNIVERSITY
BOZEMAN, MONTANA

DESCRIPTION (Adapted from applicant's abstract) : The general goal of the proposed research is to determine how information about sensory stimulus features is encoded by ensemble neural activity patterns. The preparation to be studied is the cercal sensory system of the cricket. The specific aims of this proposal are to test the following hypotheses: 1) A dynamic temporal encoding scheme is used to represent features of sensory stimuli; 2) A collective encoding scheme is used to represent sensory stimuli; 3) There is no significant loss of behaviorally relevant information across the synaptic interface between the afferent array and the 20 cell ensemble of primary sensory interneurons; and, 4) The sensory system is optimized to process typical behaviorally relevant signals from the animal's environment. The experimental database for the studies will be collected through advanced electrophysiological recording techniques. Techniques will include dual intracellular recordings from pairs of neurons and multi-unit extracellular recordings from nerves. The extracellular recordings will be achieved through the use of wire and silicon recording arrays designed specifically for these studies. The analytical approach will employ information theory , stochastic systems analysis and several engineering analyses. Neural net algorithms may be used be implement nonlinear regression analyses of complex data sets.

5F32MH011135-02
DODSON, CHAD
COGNITIVE NEUROPSYCHOLOGICAL ANALYSIS OF SOURCE MEMORY
UNIVERSITY OF CALIFORNIA
BERKELEY, CALIFORNIA

DESCRIPTION (Adapted from Applicant's Abstract):
Patients with frontal lobe damage have difficulty remembering the source or context in which information was previously learned, yet their memory for content information is relatively unimpaired. The proposed experiments provide a comprehensive analysis of the effects of frontal lobe damage on memory for source information. Specifically, the research program will 1) identify the degree of a source memory deficit in patients with frontal lobe lesions; 2) propose a new multinomiaI model of source memory; and 3) analyze implicit expressions of source information. Comparing the results from the direct and indirect tests will be very important for determining if frontal lobe patients' source memory deficit is due to the absence of this information, or if this memory deficit is due to the inaccessibility of this memorial information on tests requiring deliberate recollection (i.e., direct tests). In addition, the present project introduces an important technique for assessing source memory that emphasizes the fact that subjects can recollect a variety of information about the source of an earlier studied item. The proposed studies should help characterize the severity of the source memory deficit in frontal lobe patients, and they should also contribute to our understanding of the more general issue of source memory.

1F31MH012046-01
DORRANCE. BRIGETT
IMITATIVE LEARNING
UNIVERSITY OF KENTUCKY
LEXINGTON, KENTUCKY

DESCRIPTION (adapted from applicant's abstract) : Whether non-primates have the capacity to imitate the behavior of another animal has been a controversial topic. Claims of imitative learning by animals in their natural environment have been numerous; however, for a behavior to be considered imitation, artifacts such as social facilitation and stimulus/local enhancement must be controlled. The two-action method , developed to control for these issues and used successfully to study imitative learning in pigeons and quail, will be used in the present experiments. Experiments 1,2 and 3 will examine the quail's ability to perform conditional discriminations by observing a demonstrator. Experiments 4 will examine whether quail can learn to not imitate a behavior the lead to no reinforcer. Experiments 5, 7 and 8 will examine the quails ability to observe two distinct responses that lead to two different reinforcers and perform whichever response leads to the more desirable outcome, based on its particular motivational state. Experiments 6 and 8 will examine the effectiveness of visual access to a female as a reinforcer in imitative learning. The proposed research is expected to show further evidence that non-primates are capable of true imitative learning and will broaden our current knowledge of true imitative learning in animals.

5F32MH011566-02
DRUMMEY, ANNA
FRONTAL LOBES AND EPISODIC MEMORY DEVELOPMENT
UNIVERSITY OF MARYLAND COLLEGE PK CAMPUS
COLLEGE PARK, MARYLAND

DESCRIPTION (Adapted from Applicant's Abstract):
The proposed research will examine the relationship between frontal lobe maturation and the development of episodic memory. To this end, 4 - year-old children will participate in 6 tasks spread over 3 sessions.

These include two measures thought to reflect frontal function, two tasks indexing episodic memory, one task assessing implicit memory and one task measuring general semantic memory. We have several behavioral and electrophysiological predictions we will test. First, children's performance on the episodic memory task and putative frontal measures will be positively correlated. Second, all children, regardless of their performance on episodic and frontal tasks, will show robust implicit memory and normal levels of semantic memory.
Electrophysiological predictions include : children who are successful at the episodic memory tasks will show increased frontal lobe activation during these tasks and in a baseline condition as compared to children who are not successful. In addition, we predict increased occipital activation in the implicit memory task. However, no increase in frontal activation is predicted in this task.

5F31MH011452-02
DRUMMOND, SEAN
SLEEP DEPRIVATION EFFECTS ON MEMORY & CEREBRAL FUNCTION
UNIVERSITY OF CALIFORNIA
SAN DIEGO, CALIFORNIA

DESCRIPTION (Adapted from Applicant's Abstract):
Relatively little is known about the physiological factors that mediate the memory deficits seen with sleep deprivation (SD). This proposal aims to investigate the sequences of SD for the memory process and to determine their neurophysiological substrates. Subjects will undergo fMRI, both after a normal night of sleep and after SD, while memorizing words being presented both visually and auditorally. The change in signal intensity between the "stimulation" and "no-stimulation" conditions will be measured. It is hypothesized that SD will enhance cerebral figure - ground activation, manifested as an increase in the percent change in the signal intensity of modality-specific regions after SD, cared to after normal sleep. After imaging, subjects will be given both explicit and implicit memory tests. It is expected that explicit memory will be impaired following SD. If implicit memory is also impaired, the encoding process will be implicated as sensitive to the effects of SD. If instead , implicit memory remains intact after SD, the retrieval process will be implicated. This project will answer questions regarding the neurophysiolcgical basis for the memory deficits seen with SD, holds implications for the field of "sleepiness and performance," and may bring to light a new technique for studying the consequences of sleep loss and SD.

1F30MH011960-01A1
DUVVURI, UMA
IMAGING OXYGEN METABOLISM IN BRAIN
UNIVERSITY OF PENNSYLVANIA
PHILADELPHIA, PENNSYLVANIA

DESCRIPTION (Adapted from applicant's abstract) : Ischemic stroke is a common and devastating disorder. The long-term goal of this project is to develop a tool to study the pathophysiology of stroke and in particular the ischemic penumbra. In the ischemic core blood flow is <20 percent of normal and metabolism is almost absent. The peripheral regions also have reduced blood flow (20 to 50 percent of normal) but are only slightly hypometabolic. This region is called the " ischemic penumbra". It has been shown that this region can be salvaged with early treatment. These areas are also involved

in active protein synthesis which is thought to endow ischemic tolerance. The applicant hypothesizes that in vivo magnetic resonance imaging (MRI) of oxygen consumption can distinguish penumbral regions from infarcted regions in the setting of focal ischemia. In order to test this hypothesis the applicant proposes to develop novel MR methods to image cerebral oxygen metabolism and blood flow. The methods are based on indirect detection of the 17-0 nucleus using 1H MRI, which has already been demonstrated to be a sensitive technique. The applicant will evaluate this method in normal rats and validate it against existing methods for measuring cerebral oxygen metabolism. He will then use this method to study a reversible model of stroke involving occlusion of middle cerebral artery. The phenomenon of ischemic tolerance will be investigated by correlating MR data with immunohistochemical assays for protein expression. In this way, he hopes to be able to correlate MR images with protein synthesis. This project will greatly enhance our understanding of the pathophysiology of stroke and possibly provide a tool with which to noninvasively assess genetic therapies.

1F31MH011817-01A1
EILAND, MONICA
LOCUS COERULEUS AND RAPHE ACTIVITY IN SLEEP AND WAKING
UNIVERSITY OF CALIFORNIA
LOS ANGELES, CALIFORNIA

DESCRIPTION (adapted from applicant's abstract) : Phylogenetic comparisons between mammals and reptiles could provide important clues to the function of sleep. Features of sleep, aminergic activity and cholinergic activity common to the reptilian, avian, and mammalian lines are likely to have been present in the stem reptiles. In mammals, the adrenergic cells of the locus coeruleus (LC) and the serotonergic cells of the raphe are tonically active in waking, decrease discharge in non-REM sleep, and are silent in REM sleep. Mammals also possess two cholinergic cell populations that produce the tonic and phasic components of waking and REM. The function or evolutionary history of these discharge profiles is not known. Narcolepsy, depression and REM sleep behavior disorder may result from disturbance of these discharging profiles. Though these immunohistochemically- defined populations are also found in reptiles, their activity has not been recorded in unanesthetized reptiles. The investigators have developed methods for recording brainstem units from a reptile, the common box turtle, Terrapene Carolina, during sleep and waking behaviors. They will identify and characterize the locus coeruleus, raphe, and cholinergic cell groups of the pedunculopontine and laterodorsal tegmentum immunohistochemically and electrophysiologically. They will compare these cells' state-dependent unit activity with that of mammals in order to provide insights into mthe evolutionary significance of sleep.

5F32MH011282-03
EPELBOIM, JULIE
MATHEMATICAL MODELS OF COGNITIVE PROCESSING
STANFORD UNIVERSITY
STANFORD, CALIFORNIA

DESCRIPTION (Adapted from Applicant's Abstract):
The goal of the research is to develop a mathematical model of the mental operations used to solve problems requiring geometrical reasoning. The model's data base will consist of gaze patterns and concurrent written and verbal reports of mathematically-sophisticated subjects as they solve

geometrical problems, varying in type and difficulty. The orientations of both eyes and the head, recorded with a unique apparatus, the Maryland Revolving-Field Monitor (MRFM) will be used to determine, accurately and precisely, the location of the subjects' binocular gaze relative to the plane in which the text and figures of a geometrical problem are presented. The MRFM's uniqueness lies in the fact that such gaze patterns can be examined as the subject solves the problem naturally with the head, arms and torso free to move while the solution is worked out, narrated and written down. The MRFM requires attachments to the eyes, so its use is limited to a small set of well-informed, adult subjects. The gaze patterns of four, mathematically-sophisticated subjects, who routinely run in eye movement experiments using the MRFM, will provide the data base for developing the math model of interest. Once developed , the applicability of this model to the performance of mathematically-gifted children will be tested with children under study at Stanford. The data base for these children will be their verbal and written reports. The long range goal for this project is to develop a mathematical model of geometrical reasoning, and then use this model to study the development of mathematical sophistication. Attaining this goal has potential practical applications in both education and mental health. Namely, it can be used for (1) diagnosis of intellectual disabilities in the young and following injury to the central nervous system; (2) screening for exceptional mathematical gifts and (3) teaching less gifted individuals more efficient problem solving skills.

5F32MH011459-04
EPSTEIN, RUSSELL
REPETITION BLINDNESS AND LOCATION CODES
MASSACHUSETTS INSTITUTE OF TECHNOLOGY
CAMBRIDGE, MASSACHUSETTS

DESCRIPTION (Applicant’s Abstract): The goal of the proposed research is to use the newly discovered phenomenon of repetition blindness (RB) for locations to explore the way location is coded by the brain. RB for locations occurs when letters are rapidly presented in different locations; it is found that subjects have a relative impairment in reporting letters if a previous letter has appeared in the same location. The research proposed will simultaneously explore this phenomenon further and use it as a tool for exploring spatial codes. A number of the experiments are designed to determine what counts as “the same location” in this phenomenon. In particular, the hypothesis that the brain codes locations as distinctions between objects, or between parts of the same object, is explored. Additional experiments will examine the role of token individuation, attention, and symbolic coding in this phenomenon and attempt to map functional distinctions between location codes onto anatomical distinctions by using functional magnetic resonance imaging (MRI).

5F31MH011950-02
ERGENZINGER, EDWARD
CORTICAL EFFECTS ON THE PRIMATE SOMATOSENSORY THALAMUS
WAKE FOREST UNIVERSITY
WINSTON-SALEM, NORTH CAROLINA

DESCRIPTION (Adapted from Applicant's Abstract):
The general aim of this grant proposal is to elucidate the role of corticothalamic connections from anterior parietal cortex (APC) to the ventrobasal (VB) thalamus in the processing of somatic sensory information I adult non-human primates. Most studies concerning the

processing of sensory input have focused on the ascending flow of information from thalamus to cortex, despite the fact that descending or "feedback" projections are in many cases more numerous than "feedforward" projections and provide a substantial substrate for influencing the extraction and detection of pertinent sensory information. Most of what is known concerning the functional significance of corticothalamic projections has come from studies conducted in the visual system, which have indicated that this pathway is capable of altering the receptive field properties of thalamic sensory relay neurons. While a few studies have attempted to discern the influence of corticothalamic input on the responses of relay neurons in the VB thalamus, they have failed to address the fact that substantial difference exist in the anatomical and functional organization of somatosensory systems between mammals. This application addresses the functional significance of corticothalamic connections within the somatosensory system of adult macaques by examining whether pharmacological interference of corticothalamic neuronal activity from APC alters the response properties of VB relay neurons. In addition , this application directly addresses the mechanisms through which these changes might be taking place by examining whether these changes are associated with alterations in markers for glutamate or GABA or their receptors. It is hoped that this research will provide a greater understanding of the complexity of sensory processing by addressing "top-down" influences over normal activity as well as changes in neuronal responses associated with experience or injury-induced reorganizational plasticity.

1F31MH012282-01
ERICKSON, SUSAN
PATTERNED THALAMIC AFFERENTS AND PREFRONTAL CIRCUITRY
UNIVERSITY OF PITTSBURGH
PITTSBURGH, PENNSYLVANIA

DESCRIPTION Adapted from applicant's abstract) : The precise organization of individual neurons into neural circuits is essential for all neural functions. There is increasing evidence that such debilitating mental diseases as schizophrenia and autism may result from failure of neural circuits to develop properly. A common feature of neural circuits is the convergence of several inputs onto a single target. This convergence requires that a neuron not only find and synapse with the proper postsynaptic cell, but also appropriately share this target cell with other inputs. In some cases, the functioning of the circuit critically depends on the precise connection of the presynaptic cell onto a specific sub-region of the postsynaptic neuron, for example, onto a single dendritic branch or onto the initial segment of the axon. Studying this development in a simple nervous system not only allows one to learn the mechanisms involved, but also may eventually allow one to interpret the functional consequences of inappropriate development. The experiments proposed are designed to characterize the connection between a subset of neurons involved in a specific behavior, the local bending reflex, in the medicinal leech. Specifically, the connection from each of two pairs of excitatory interneurons onto a shared postsynaptic motor neuron will be studied. The precise location of each connection will be identified by photoablation of branches and subsequent intracellular electrical recording of the presynaptic and postsynaptic cells. The time at which the connection first develops will be determined by using paired electrical recordings at several different embryonic ages. Finally, the role of interactions among

presynaptic neurons, as well as between the presynaptic neuron with specific postsynaptic branches, in generating precise connections, will be assessed by ablating entire presynaptic cells or individual postsynaptic branches during development, before any connections are made.

1F32MH12029-01
ESCH, TERESA M
DEVELOPMENT OF SPECIFIC NEURONAL CONNECTIONS IN LEECH
UNIVERSITY OF CALIFORNIA SAN DIEGO
SAN DIEGO, CALIFORNIA

DESCRIPTION (Adapted from applicant's abstract) : The precise organization of individual neurons into neural circuits is essential for all neural functions. There is increasing evidence that such debilitating mental diseases as schizophrenia and autism may result from failure of neural circuits to develop properly. A common feature of neural circuits is the convergence of several inputs onto a single target. This convergence requires that a neuron not only find and synapse with the proper postsynaptic cell, but also appropriately share this target cell with other inputs. In some cases, the functioning of the circuit critically depends on the precise connection of the presynaptic cell onto a specific sub-region of the postsynaptic neuron, for example, onto a single dendritic branch or onto the initial segment of the axon. Studying this development in a simple nervous system not only allows one to learn the mechanisms involved, but also may eventually allow one to interpret the functional consequences of inappropriate development. The experiments proposed are designed to characterize the connection between a subset of neurons involved in a specific behavior, the local bending reflex, in the medicinal leech. Specifically, the connection from each of two pairs of excitatory interneurons onto a shared postsynaptic motor neuron will be studied. The precise location of each connection will be identified by photoablation of branches and subsequent intracellular electrical recording of the presynaptic and postsynaptic cells. The time at which the connection first develops will be determined by using paired electrical recordings at several different embryonic ages. Finally, the role of interactions among presynaptic neurons, as well as between the presynaptic neuron with specific postsynaptic branches, in generating precise connections, will be assessed by ablating entire presynaptic cells or individual postsynaptic branches during development, before any connections are made.

1F31MH012031-01A1
EVANS, JENAFER
ANGIOTENSIN II--A CNS NEUROMODULATOR
UNIVERSITY OF FLORIDA
GAINESVILLE, FLORIDA

DESCRIPTION (Adapted from Applicant's Abstract):
Angiotensin II (Ang II) plays a major role in the central nervous system in the regulation of memory, behavior, and learning. Centrally and peripherally, Ang II facilitates neurotransmission by enhancing norepinephrine (NE) release from catecholaminergic nerve terminals and prohibiting reuptake. Activation of Ang II type I (AT1) receptors in the hypothalamus and brainstem lead to physiological changes including increased drinking, increased baroreceptor function, and alterations in arterial pressure. Little information is available regarding the modulatory actions of Ang II on neuronal ionic currents which are the basis of neuronal action potentials. Knowledge of ionic current modulation by Ang II is therefore of great interest due to the

fundamental importance of the frequency and firing patterns of action potentials to all physiological events mediated by a given neuron. Disruption of the intracellular signaling events responsible for the modulatory actions of Ang II would lead to alteration of neuronal activity. Due to its importance as an intracellular messenger and its role in neurotransmitter release, the specific aims set forth in this proposal focus on neuronal Ca2+ current and its modulation by Ang II through the AT1 receptor. The aims are: 1) Biophysically and pharmacologically characterize the Ca2+ channels expressed in cultured neonatal rat hypothalamic neurons. 2) Determine which Ca2+ channel subtypes are modulated by Ang II. 3) Determine the intracellular pathways responsible for the Ang II modulation of Ca2+ current. 4) Compare and contrast the effects of Ca2+ channel blockers on Ang II and KC1-induced norepinephrine release. The results gathered from this study will help to elucidate the effects of Ang II on different neuronal Ca2+ channel subtypes and enhance our knowledge of the regulation of norepinephrine release in the brain and thus, the central control of arterial blood pressure.

1F32MH012422-01
FANCSIK, ANDRAS
NEUROSTEROID REGULATION OF GABA CURRENTS IN HYPOTHALAMUS
TULANE UNIVERSITY OF LOUISIANA
NEW ORLEANS, LOUISIANA

DESCRIPTION (Adapted from applicant's abstract) : The recent indications that hormone-replacement therapy might improve cognitive abilities and delay the onset of Alzheimer's disease in post-menopausal women has led to increased research on neural mechanisms of action of estrogens. However , there seems to be little research on sex steroids' regulation of neuropeptides such as vasopressin (VP) in the hippocampus, despite extensive evidence these substances have numerous cognition-enhancing and neurotrophic properties and are often regulated by sex steroids. These proposals build on evidence that VP is regulated by both estrogens and androgens in the hippocampus and that intrahippocampal VP has many of the cellular and behavioral properties ascribed to sex steroids. The proposed experiments are designed to examine causal relationships and to begin determining if some of the neuroprotective and cognition-enhancing properties of gonadal steroids result from their regulation of VP in the hippocampus. These experiments seek to differentiate the influences of estrogenic and androgenic metabolites of testosterone in the male, and also examine the affects of seasonal changes in light on the sensitivity of VP cells to steroids. The results could offer clues to seasonal affective disorders and to differential responses to hormone-replacement therapy in humans.

1F31MH11662-01
FARKAS, FRANK W
CIRCADIAN OUTPUT SIGNALS FROM THE SCN
NORTHWESTERN UNIVERSITY
EVANSTON, ILLINOIS

DESCRIPTION (Adapted from applicant's abstract) : While aging and several pathologies, especially depression, are associated with more aberrations in circadian rhythms, the underlying points of disruption in the circadian system are unknown. A great deal of research currently focuses on the genetic and molecular events generating circadian oscillations within the suprachiasmatic nucleus (SCN), the master circadian pacemaker of animals. In addition,

substantial information has accumulated on phase-altering input signals to the SCN and on factors disrupting the entrainment of the pacemaker. However, little is currently known about the output signals and targets of the SCN and the role played by disruption of these signals in circadian aberrations. Since past research suggests that humoral secretions from the SCN or under the control of the SCN play significant roles in transmitting circadian signals to the rest of the brain, this project seeks to elucidate the role of the circadian cycle of vasopressin secretion from the SCN into the cerebrospinal fluid (CSF), as well as the significance of age-related declines in circadian melatonin secretions from the pineal gland, a structure directly and neurally controlled by SCN. The project involves SCN lesions of Golden hamsters (Mesocricetus auratus) to eliminate endogenous circadian signals and rhythms. The circadian rhythm of vasopressin in the CSF will then be restored through intracerebroventricular infusions to study the effects of this regimen on daily activity patterns in the absence of daily light cycles. In a separate study, the nighttime melatonin levels of old hamsters will be restored to the robust levels of young hamsters through subcutaneous infusions. Activity rhythms will be monitored before and during the infusions to examine if melatonin can enhance circadian rhythms in old animals similar to recent observations with a melatonin agonist. Since altered humoral signals are currently much easier to correct thaN neural signals, these and related studies could suggest means of correcting clinical disorders of circadian rhythms and the sequelae of these disorders.

5F31MH011675-02
FEIDLER, JORDAN
MODELING THE MECHANISMS OF DIRECTION SELECTIVITY
UNIVERSITY OF PITTSBURGH
PITTSBURGH, PENNSYLVANI

DESCRIPTION (Adapted from Applicant's Abstract):
Computer modeling will be used to elucidate the mechanisms that underlie direction selectivity (DS) in simple cells of primary visual cortex. DS serves as a good model for understanding the more general problem of how the brain performs behaviors that require precise temporal information. This problem is highly relevant clinically; for example the disruption of temporal processing is an important factor dyslexia. In visual cortex, a neuron's DS derives from inputs that have their own spatial and temporal structure. These inputs may arise from three sources: the lateral geniculate nucleus (LGN) and other excitatory or inhibitory cortical cells. A key problem this study will address is to identify those spatiotemporal relationships among LGN afferents and interacting cortical neurons which initially create or enhance DS. Major project goals will be to: (1) Develop a computer model that investigates the ability of lagged and nonlagged LGN cells alone to establish a directional preference in area 17 simple cells. (2) Incorporate into the model intracortical excitatory and inhibitory connections and examine their ability to establish or enhance a directional preference. (3) Simulate the development of direction selectivity through Hebbian learning. (4) Evaluate the validity of the computer model by comparing the response of model cortical units with those of actual cat area 17 simple cells for a variety of test stimuli.

5F32MH11373-03
FERREE, THOMAS C

NEURAL COMPUTATION IN C ELEGANS CHEMOTAXIS
UNIVERSITY OF OREGON
EUGENE, OREGON

DESCRIPTION (Adapted from applicant's abstract) : Compartmental modeling and neural network optimization can be used in conjunction to understand the neural computations which underlie animal behavior. The proposed research focuses on chemotaxis in the nematode Caenorhabditis elegans, whose neuroanatomy is known in great detail. Recently the sponsor has developed experimental techniques which enable making the necessary electrophysiological recordings. It is now possible for the first time to construct a realistic neural network model with the objective of understanding the neuronal basis of neural computation in this animal. The chemotaxis circuit is known with confidence. Compartmental models of individual neurons will be constructed based on known morphologies and measured biophysical parameters. Synaptic functions will either be measured or assumed similar to Ascaris suum, and synaptic weights will be assumed proportional to the number of connections between neurons. Brute force search and/or neural network optimization will be used to determine the polarity of synaptic connections, and the resulting model will be tested by comparing simulated laser ablations done in the model with real laser ablations done in the animal. The goal is to reveal the mechanisms by which C. elegans carries out neural computations in spite of inherent neuronal noise and other limitations associated with its extremely small size.

5F30MH010762-04
FISHER, CAROLINE
DEPARTMENT OF PHARMACOLOGY
BOSTON UNIVERSITY
BOSTON, MASSACHUSETTS

DESCRIPTION (Adapted from Applicant's Abstract):
This proposal sets forth the design and creation of two highly specific diphtheria-based neurotoxins paralleling previous work with IL-2. Each fusion toxin will consist of an abbreviated diphtheria toxin bound to the neuropeptides substance P or neurotensin. Thus when the extended peptide bind to its receptor, the diphtheria toxin will be incorporated into the neuron and destroy it. The ability to lesion specific neurons confers the means of directly observing which neurons bind the peptide while also observing the functional consequences in vivo of eliminating these neurons. Initial steps in the production of the toxin have entailed modifying a plasmid encoding an abbreviated form of the diphtheria toxin. Oligonucleotides coding for the substance P precursor peptide, substance P-glycine have been inserted. The enlarged plasmid was transformed into E. coli bacteria and these bacteria were induced to express the protein which will be reacted with an enzyme to cleave the glycine from the end of substance P and thereby make it recognizable to cells bearing substance P receptors. The neurotensin toxin will be produced similarly. The toxins will be extensively characterized in vitro and in vivo, with the ultimate goal of using them experimentally to ascertain neural function. The ability to selectively lesion neurons expressing receptors for these peptides should lead to better understanding of the function of these peptides as neurotransmitters, and may help to elucidate their role in mental disorders. The substance P fusion toxin may also have clinical applications in the treatment of chronic pain and inflammation.

7F31MH011764-02

FONTAINE, REID
RESPONSE DECISION IN AGGRESSIVE/NONAGGRESSIVE YOUTHS
DUKE UNIVERSITY
DURHAM, NORTH CAROLINA

DESCRIPTION (Adapted from Applicant's Abstract) : The primary goal of the proposed set of studies is to examine how children's response decision patterns (i.e., response evaluation and selection), especially within moral and esteem dimensions, relate to the development of chronic aggressive behavior, early social maladjustment, emotional states, and physiological reactivity. Response decision patterns have to do with how youths tend to evaluate and select from alternative ways in which to respond to a social cue. A model of response evaluation and selection is proposed herin and is operationalized according to social information-processing, a theoretical framework of social competence and the order of cognitive processes which may function in response to situation-specific, social stimuli (developed by the sponsor: Dodge, 1986, 1993; Crick & Dodge, 1994).
This research program has been designed to examine the interrelations of (a) moral reasoning and dimensions of response evaluation, (b) interpersonal adjustment (maladaptive peer relations), (c) affective influences, and (d) physiological arousal, and how these operaitons relate to the early development of (e) aggressive and deviant behaviors. The current proposal, involving a progression of three studies, will include these main analyses. (1) the role of response evaluation in aggressive and deviant behavioral tendencies, (2) the potential mediation of response evaluation styles in the progression from early social maladjustment to later conduct problems, and (3) the degree to which response evaluation factors into aggressive behaviors which are based partially on anger and physiological arousal.

5F31MH011812-02
FRANOWICZ, MATTHEW
MODULAR INTERACTION IN PREFRONTAL CORTEX
YALE UNIVERSITY
NEW HAVEN, CONNECTICUT

DESCRIPTION (Adapted from Applicant's Abstract):
Prefrontal cortex (PFC) participates in a network with other cortical and sub-cortical structures, which serves to hold information active over short periods of time. This "neuronal glue" of consciousness is responsible for our ability to plan, read, and reason and reaches its greatest cortical expanse in humans. Evidence suggests that PFC contains cortically separate working memory domains for aspects of vision, audition, and language. What is the nature of the interaction between these areas? The aim of the proposed experiments is to look at two of these areas, 4 and 12, which has been identified as working memory centers for spatial and object aspects of visual stimuli respectively. Previous research in our laboratory has suggested that corticocortical connections between these regions exist. In the proposed experiments rhesus monkeys will be trained on a working memory task in which the animal encodes either the form or location of a visual stimulus or both. Multi-electrodes in these areas will record activity simultaneously. It is hypothesized that although different aspects of visual information arrive at PFC in parallel, interactions will exist between visual sub-modalities. This research may reveal the dynamic properties of PFC in terms of its ability to integrate information about stimuli that had been initially segregated in primary visual cortex. Finally, this investigation could offer

physiological mechanisms through which different features distributed across cortex could be unified into a consciously perceived item (i.e. the "binding problem").

1F31MH011839-01A1
FREEMAN MARC
DARE--OLFACTORY BEHAVIORAL MUTANT WITH HORMONE DEFECTS
YALE UNIVERSITY
NEW HAVEN, CONNECTICUT

DESCRIPTION (Adapted from applicant's abstract) : Dare mutants behave abnormally in response to olfactory repellents and have defects in male courtship behavior. The long-term goal of this project is to characterize the role of dare in the function and development of the Drosophila olfactory system. Dare encodes the Drosophila homologue of adrenodoxin reductase (AR), which has been shown in mammals to be essential for the key, rate limiting step in the synthesis of all steroid hormones. Dare is the first mutant with a lesion in the steroid biosynthetic pathway and links steroid hormones with sensory behavior. Several new dare alleles will be tested in a variety of behavioral and electrophysiological olfactory paradigms. Nervous system morphology in dare mutant animals will be observed at several developmental stages in an attempt to identify the nature, timing, and extent of any abnormalities. I will attempt to rescue behavioral and developmental defects using a transformant line harboring a heat shock-inducible AR cDNA construct (hs-AR). In the absence of full phenotypic rescue by hs-AR, I will generate flies harboring a genomic fragment which covers the AR gene for similar experiments and begin a screen for new dare alleles. After dare has been rigorously identified as AR , developmental Northern analysis and in situ hybridizations to RNA in tissue sections will be used to determine the pattern and developmental time course of dare expression. Time permitting, I will screen for a temperature-sensitive allele of dare and attempt to rescue male courtship defects by the directed expression of dare in male pheromone-producing tissues.

5F32MH011655-02
FREEMAN, DAVID
PHYSIOLOGY OF CIRCANNUAL RHYTHMS
UNIVERSITY OF CALIFORNIA
BERKELEY, CALIFORNIA

DESCRIPTION (Adapted from Applicant's Abstract):
The proposed research evaluates the impact of several physiological stimuli on circannual rhythms of golden-mantled ground squirrels, including the role of endogenous circannual fluctuations in body temperature on circannual variations in circadian organization and metabolic rate. The decrease in body temperature normally associated with the hibernation season will be blocked and the presence of circannual variations in circadian entrainment and metabolic rate determined. The role of prenatal photoperiod in the timing/ generation of circannual rhythms of young squirrels will also be examined in squirrels kept either in constant light, to eliminate photoperiod cues, or a simulated natural photoperiod during gestation. The timing and/ or presence of circannual rhythms in the offspring of these females will be examined. Neural sites at which testosterone (T) suppresses hibernation will be examined in male squirrels implanted with cannulae containing T into neural sites that contain T receptors and implicated in

thermoregulation. The inhibitory role of the suprachiasmatic nucleus (SCN) in circannual timing of hibernation and reproduction in male squirrels will be examined to determine if this nucleus functions similarly in males as in females to limit hibernation and reproduction to particular times of year. This research may help in the development of interventions for treating human disorders that have a circannual basis.

1F32MH012127-01
FRIEDMAN, MICHAEL
EMOTION, SOCIAL SUPPORT & THE COURSE OF MAJOR DEPRESSION
RHODE ISLAND HOSPITAL
PROVIDENCE, RHODE ISLAND

DESCRIPTION (Applicant's abstract) : This investigation will utilize a prospective design to examine the impact of spousal expressed emotion (i.e., critical, hostile attitudes towards an identified patient by a spouse) and spousal support (i.e., constructive, helpful attitudes and behaviors towards an identified patient by a spouse) on the course of major depression. While expressed emotion has been hypothesized to be associated with a poorer course of depression, results studying this relation have been mixed. One possible reason for the inconsistent findings is that expressed emotion has been studied independent of other aspects of the marital relationship, such as spousal support. However, recent social support research suggests that spousal criticism and support are independent aspects of marital functioning, not simply two poles of a common underlying latent variable, and have differential effects on psychological distress. Currently, the relation between spousal expressed emotion and support, and their independent and interactive effect on the course of major depression, has not been studied. Developing a better understanding of the relation between spousal expressed emotion and support, and the course of depression would have direct implications for the treatment and prevention of this disorder. The current proposal will examine the effects of spousal expressed emotion and support using a naturalistic, prospective design. One hundred patients will be recruited during an episode of major depression. Symptom patterns will be assessed initially at baseline, and again at a 9-month follow-up, utilizing self-report and interview-based measures. Spousal expressed emotion and support will be assessed using comprehensive interview-based and self-report measures at baseline. Analyses will address three main study goals. First, this study will examine whether spousal expressed emotion and support are actually independent constructs, or rather two poles of a common underlying latent variable. Second, we will determine the independent impact of both spousal expressed emotion and support on the course of major depression. Finally, we will investigate the interactive relation between these constructs, particularly whether spousal support buffers the effects of expressed emotion on the course of depression.

1F31MH011781-01A1
FRIEL, LARA
CNS DOPAMINERGIC TRANSPLANTS--HOST IMMUNE RESPONSES
FINCH UNIV OF HLTH SCI/CHICAGO MED SCH
CHICAGO, ILLINOIS

DESCRIPTION (Applicant's Abstract) : The applicant's ultimate career goal is to combine research and clinical practice in an academic setting where she also will be able to participate in the training of residents and medical students. This proposal, which will serve as her dissertation, focuses on

the host immune response to intracerebral mesencephalic grafts in an animal model of Parkinson's disease. Skills she will learn in the course of training include stereotaxic surgery, fetal brain dissection, neuronal cell culture, in situ hybridization, immunohistochemistry, 6-OHDA lesioning, behavioral measurements, and proper design and interpretation of experiments. These skills, along with the multidisciplinary training offered in the Neuroscience Department, will provide a foundation for her development as a clinical research scientist with interests in neuroimmunomodulation and neuroendocrine-immune interactions. In addition , this project is suited to her career goals in that she will learn these specific skills in the process of conducting a project with clinical relevance. In terms of the project itself, low cell survival confounds efforts to utilize fetal tissue transplantation as a replacement therapy in human diseases, such as Parkinson's Disease. The death of neurons in developing ventral mesencephalic grafts was assumed to be necrotic until recent efforts revealed that these cells also undergo apoptoic death. Immune-mediated rejection of intracerebral transplants may impede significantly the survival of histoincompatible grafts; in fact, rejection has been demonstrated in rodent and non-human primate transplantation paradigms. Since alloreactive cytoxoxic T cells are important in peripheral graft rejection and can induce apoptotic death in their target cells, this proposal will attempt to: 1) determine whether allogeneic lymphocytes contribute to apoptotic death of mesencephalic cells in a co-culture model, 2) characterize and quantify immune cell populations recruited to the area of the graft in vivo, and 3) to determine whether lymphocytes in and around the graft lead to increased apoptotic death of grafted cells. Since the host's immune response may contribute to the death of transplanted neurons, utilization of knowledge gained in detailed studies of this response ultimately may lead to means by which survival can be increased. The applicant's long term objectives are to assess the contribution of the host immune response to the death of mesencephalic neurons in an effort to gain a greater understanding as to whether immunosuppression is necessary in neural transplantation.

1F32MH011921-01A1
FROST BELLGOWAN, PATRICK
FUNCTIONAL MRI OF HUMAN MEMORY SYSTEMS
MEDICAL COLLEGE OF WISCONSIN
MILWAUKEE, WISCONSIN

DESCRIPTION (Adapted from applicant's abstract) : The purpose of this project will be to understand the role of the medial temporal lobes (MTL) in the encoding and retrieval of several different forms of memory, using functional magnetic resonance imaging (fMRI). Encoding process manipulations will be used to determine lateralization of memory function, whereas manipulations of the type of associations available during encoding of a stimulus event will be used to delineate the stimulus properties that elicit MTL participation and storage in long-term memory. During fMRI scanning, subjects will perform either a semantic decision, spatial discrimination, facial decision, or combination of semantic and spatial decision tasks alternated with a shape decision baseline task. Performance of these tasks will induce incidental encoding of the relevant stimulus even in long-term memory. Another scanning session will be conducted to test the recognition of the stimulus event in each form of memory task and to determine the MTLs role in the retrieval phase of memory. Within- subject t-tests will be conducted between each target and control task, average activations maps will be produced, and region of interest comparisons will

be conducted both between and within groups. The applicant predicts that the MTL will show lateralization of function for linguistic and spatially demanding tasks and that activation of this region will be specific to encoding stimulus events that involve configural integration of intra-stimulus elements in forming the association.

1F31MH012075-01
FUGGER, HEATHER
ERA AND LEARNING AND HIPPOCAMPAL FUNCTION
UNIVERSITY OF VIRGINIA
CHARLOTTESVILLE, VIRGINIA

DESCRIPTION (Developed from applicant's abstract) : This research is designed to yield information about estradiol activation of the estrogen receptor (alpha) on spatial learning, retention of avoidance learning and excitation of hippocampal electrophysiology. The proposed studies will contribute to the understanding of changes in hippocampal-dependent behaviors and hippocampal synaptic function in relation to gonadal steroids. Results from the experiments will be beneficial to understanding the role of estradiol activation of the estrogen receptor (alpha). In addition, results from the proposed experiments will provide a fundamental backbone to the knowledge of estrogenic effects during memory loss associated with aging and Alzheimer's disease. Undoubtedly, any information obtained regarding the mechanisms of estradiol action will lend insight into several women's health issues such as changes following menopause.

5F31MH011766-02
GABLE, SHELLY
APPROACH AND AVOIDANCE--DISPOSITIONS AND DAILY EVENTS
UNIVERSITY OF ROCHESTER
ROCHESTER, NEW YORK

DESCRIPTION (Adapted from Applicant's Abstract):
The proposed program of research seeks to disentangle the effects of dispositional tendencies and daily events on well-being and to understand the interaction of these constructs as they relate to predicting psychological and physical health. Specifically, the studies described in this proposal were designed to investigate the relationships among people's dispositional sensitivities to approaching positive outcomes and avoiding negative outcomes, daily events, and well-being. The studies are aimed at increasing our understanding of how both between person differences and within-person-variability combine to predict psychological health and self-reported physical symptoms. The research design is aimed at assessing dispositional tendencies, measuring daily events and well-being for 21 days, and assessing psychological health and self-reported physical symptoms. The methods allow for simultaneous examination of trait and state factors involved in well-being, and data will be analyzed with statistical techniques designed for hierarchically nested data such as these.

5F32MH011937-02
GARRETT, AMY
MEMORY AND EMOTION IN PTSD PATIENTS AND CONTROLS
UNIVERSITY OF CALIFORNIA
DAVIS, CALIFORNIA

DESCRIPTION (Adapted from Applicant's Abstract):

Several behavioral studies have shown that memory is often enhanced for emotional stimuli in normals. Compared to normals, patients with Post-Traumatic Stress Disorder (PTSD) exhibit selectively enhanced recall for trauma-related material. but show deficits in recall of neutral stimuli. This suggests a functional abnormality of the emotional memory system in PTSD. Previous neuroimaging and neurobioligical studies have suggested that the amygdala, hippocampus, posterior cingulate, retrosplenial cortex, and prefrontal cortex are involved in the acquisition and retrieval of emotional episodic memory. This study uses fMRI to investigate neurofunctional differences between patients with PTSD and controls during the presentation of emotional and neutral stimuli. Subsequent recall and recognition of the stimuli will describe individual and group differences in memory performance. We hypothesize that PTSD subjects, compared to controls, will show increased amygdala and posterior cingulate cortex activation in response to threatening stimuli, but decreased hippocampus activation in response to neutral stimuli. Also, performance on the recall task will be related to the degree of activation in the amygdala and hippocampus. These studies will contribute to the understanding of how the brain enhances memory of emotional stimuli and how this memory for emotional and neutral stimuli may be altered in PTSD. These data will provide the foundation for a systematic program of clinical neuroscience research in PTSD.

1F31MH012098-01
GASPERONI, TIMOTHY
BRAIN ABNORMALITIES--TWINS DISCORDANT FOR SCHIZOPHRENIA
UNIVERSITY OF PENNSYLVANIA
PHILADELPHIA, PENNSYLVANI

DESCRIPTION (Applicant's abstract): A series of family and adoption studies has provided compelling evidence that schizophrenia is a substantially heritable disorder. While little controversy exists over the significance of genetic factors, the precise mode of inheritance and the nature of the genetic diathesis remain to be determined. One of the more promising approaches to resolving these issues is to study the well family members of patients with schizophrenia. Since schizophrenia has a nontrivial, heritable component, a portion of such unaffected relatives may exhibit neuroanatomical abnormalities associated with familial risk for the disorder. These so-called "endophenotypic" markers are likely to be closer to the mechanism of gene action and may ultimately be used to facilitate genetic linkage studies and the design of prophylactic interventions. Perhaps the most powerful extension of this logic is the discordant monozygotic twin paradigm. Because these individuals share a common genome, this approach affords the unique advantage of identifying brain abnormalities that can be confidently attributed to environmental factors and/or the presence of the disease process. In this vein, I am proposing to examine data from a structural magnetic resonance imaging study of normal and discordant monozygotic twins to determine whether distinct patterns of cerebral pathology are associated with disease and vulnerability-specific components of schizophrenia. I will also combine quantitative MRI data with prospectively-obtained obstetric and birth records to assess the contribution of perinatal complications to differences in brain structure between discordant twins.

1F31MH012240-01
GIBBONS, AMANDA

RESEARCH TRAINING PROPOSAL
JOHNS HOPKINS UNIVERSITY
BALTIMORE, MARYLAND

Description (Adapted from applicant's abstract): The training program on behavioral research for HIV/AIDS prevention. While there have been some long-awaited breakthroughs in drug development with the utilization of protease inhibitors, there still is no cure or vaccine for HIV disease. Therefore, prevention education and intervention programs remain essential to slow the transmission and geographic spread of HIV. Research will be performed on primary prevention tactics to identify and evaluate AIDS-intervention strategies and to target specific at-risk populations in need of these interventions. To achieve this goal, data from quantitative and qualitative sources will be employed to measure changes in HIV knowledge, beliefs, and behaviors, and to determine societal factors that may be barriers to prevention efforts. The intervention components which will be assessed include: social determinants of health and risk behaviors, the component of high-risk behaviors within specific communities, the impact of different community-based behavior change programs, and the impact of human rights and other societal factors on risk behaviors pertaining to HIV. Adolescent women from developing countries will be the focus of the research, in attempt to determine characteristics that put this population at risk. The research will examine the psychosocial determinants for HIV risk behaviors and investigate intervention programs that would enable the health care professional to target at-risk populations as a whole, rather than individually. This task would encompass the understanding of what crucial components identify at risk populations, how these components differ in various settings, and how the social structures allow for, and hinder, behavioral change. The goal of the research will be to develop long-term prevention methods that address relapse into risky behaviors.

1F32MH11898-02
GILLARD, ELIZABETH R
ELECTROPHYSIOLOGY OF MELANIN CONCENTRATING HORMONE
UNIVERSITY OF ALBERTA
EDMONTON, CANADA

DESCRIPTION (adapted from applicant's abstract): Understanding the central mechanisms controlling eating behavior is important for understanding how the nervous system may contribute to the eating and body weight disorders common in Western society. Evidence implicates the lateral hypothalamus (LH) as a key site in the neural control of food intake. This project will examine the cellular mechanisms by which melanin-concentrating hormone (MCH), a peptide produced almost exclusively by LH neurons, participates in the control of eating behavior using the rat as a model system. Specifically, the anorectic effects of MCH will be tested in vivo, to determine which LH sites are most sensitive to the effect of MCH, and the time of the photoperiod in which MCH maximally induces eating. The effects of MCH in rats feeding in response to the onset of the dark cycle, food deprivation, or LH glutamate receptor stimulation (all of which induce eating) will be tested to determine conditions in which MCH might play a role as a physiological mediator of eating suppression. The in vitro brain slice preparation will be used to address the effects of MCH on glutamatergic and GABAergic synaptic transmission in the LH, with an aim to identifying the cellular mechanisms by which MCH in the LH affects Feeding. In addition, interactions of MCH with the feeding-stimulatory peptide neuropeptide Y will be examined in LH neurons in vitro, along with the possible intracellular mediators of MCH's effects on synaptic transmission. Given the almost exclusive localization of MCH to LH neurons. this work may have unusual potential to lead to the development of powerful and scientific treatments for eating disorders.

5F32MH011509-03
GINER-SOROLLA, ROGER S
IMMEDIATE AND DELIBERATIVE AFFECTIVE ATTITUDES
UNIVERSITY OF VIRGINIA CHARLOTTESVILLE
CHARLOTTESVILLE, VIRGINIA

DESCRIPTION (Adapted from applicant's abstract): The proposed research will clarify the relation between two different constructs previously grouped under the term "affective attitude": immediate affect, or a quick, unconstructed positive or negative response to an object; and deliberative affect, or the positivity or negativity of specific emotions evoked by thinking about an object. Six studies are proposed. Studies 1 and 2 will examine the relations between measures thought to access immediate and deliberative affect, using correlation and structural analytic techniques to assess the discriminant validity of these two constructs. Studies 3 and 4 will induce affectively based attitudes either by immediate or deliberative methods, in order to show that measures of immediate affect are more sensitive to immediate manipulations of affective attitude, and that measures of deliberative affect are more sensitive to deliberative manipulations. Study 5 will examine the consequences of the deliberative/immediate distinction for the process of deliberative, affectively focused introspection; Study 6 will similarly extend this distinction into the areas of affective and cognitive persuasion, making novel predictions about the efficacy of different persuasive methods upon attitudes with different bases.

5F32MH011293-03
GLASSMAN, NOAH
NONCONSCIOUS PROCESSES IN TRANSFERENCE
NEW YORK UNIVERSITY
New York, New York

DESCRIPTION (Adapted from applicant's abstract): Personality and clinical theorists posit that past experiences with significant others may influence present-day interactions with individual's in one's life or with a therapist in psychotherapy (Bowlby, 1969; Freud, 1912/1958; Sullivan, 1953). Hence, understanding the activation and application of mental representations of significant others in social perception, i.e., transference, is of clinical importance. The proposed research will extend previous work on the conscious evaluations in relation to a target person (Andersen & Baum, 1994; Andersen & Cole, 1990) --by examining nonconscious information processing in transference phenomena. Three studies are proposed, the latter two of which will be developed further during the fellowship on the basis of relevant training received. These studies will examine, respectively: (1) the affective and motivational consequences of activating significant other representations outside of conscious awareness; (2) the triggering of goal-directed action based on the nonconscious activation of significant-other representations; and (3) the respective contributions of consciously controlled and nonconscious processes on transference. Using state-of-the-art methods, this research will contribute to a greater understanding of transference, and will have implications for the nature of associative links between individual-person representations, affects, and motivational constructs in information processing models. Moreover, the research will enable in-depth hands-on training in the examination of nonconscious processes in social cognition.

1F31MH012171-01

GOLDSTEIN, MICHAEL
RECEIVERS AND HUMAN INFANT VOCAL LEARNING
INDIANA UNIVERSITY
BLOOMINGTON, INDIANA

DESCRIPTION (Applicant's Abstract): When viewed in social context, early vocal behavior is an instrument of learning. Through the activity of vocalizing and observing the reactions of others, infants acquire an understanding of the contingencies that structure communicative interaction. The purpose of the proposed research is to elucidate the role of the receiver in human vocal learning. Adapting methods used successfully in studies of animal communication, the proposed research will address social contributions to vocal learning by assessing adult responses to playbacks of infant behavior. In Project 1, playbacks of infant behavior will be used to specify the acoustic determinants of maternal responses to prelinguistic vocalizations. To validate and extend the initial findings, additional playback studies will focus on the effects of perturbations of vocal characteristics. Natural and synthetic vocalizations will be used to model the changes in vocal behavior exhibited in Down syndrome infants that create differences in the development of social response which may facilitate communicative dysfuntion. In Project 2, a second playback series will assess the influence of experience on responsivity to infant sounds. Follow-up studies will assess the effectiveness of training on the acquisition of experienced maternal patterns of responding. Taken together, these studies explore the origins of communicative competence as emergent from the system of sender and receiver, and will increase our knowledge of the contingencies that frame communicative interaction in both typically-and atypically developing populations.

1F32MH012117-01
GOTTER, ANTHONY
REGULATION OF CLOCK GENE EXPRESSION BY ANTISENSE RNA
MASSACHUSETTS GENERAL HOSPITAL
BOSTON, MASSACHUSETTS

DESCRIPTION (Adapted from applicant's abstract): This work will investigate the function of an endogenous antisense RNA in regulating per clock gene expression and, therefore, behavioral rhythms in the giant silkmoth. The full-length cDNA for the antisense transcript will be determined by first mapping a minimal sequence by ribonuclease protection assay followed by 5' and 3' RACE. This will delineate the possible regions of hybridization that might occur between these two transcripts in vivo. The functional importance of RNA duplex formation will then be investigated by administering exogenous antisense oligonucleotides designed to disrupt RNA-RNA interactions while examining alterations in per mRNA and protein oscillation as well as behavioral rhythms. Similar experiments utilizing antisense oligonucleotides will be done to attenuate the translation of any proteins that may be encoded by the novel antisense cDNA. Duplex formation between the sense and antisense per transcripts and the disruption of these by exogenous oligonucleotides will be confirmed by modified ribonuclease protection assays. These studies will lend insight into the molecular mechanisms of circadian behavior and contribute to our understanding of sleep disorders and circadian-based susceptibility to disease.

1F31MH012286-01
GREENFIELD, ELLIOT
BIOLOGICALLY REALISTIC NEURAL NETWORK MODELS

UNIVERSITY OF CALIFORNIA
BERKELEY, CALIFORNIA

The main goal of the research is to work to bridge the gap between neural network theory and experimental neurobiology by developing biologically realistic neural network models. These models will reflect the architecture of real neural networks by having dilute, asymmetric connections. The resulting dynamics, which include fixed point, periodic, and chaotic attractors, have all been observed experimentally. Using information theory and nonlinear dynamical systems theory in conjunction with computer simulations, the connection will be made between the network's dynamics and its ability to perform various types of computations. Based n these results, neurological disorders, including Alzheimer's disease and epilepsy, will be modeled as deviations from the "healthy" dynamics which allow the network to unction.

1F31MH012094-01
GREWEN, KAREN
HOPELESSNESS AND PESSIMISM--HYPERTENSIVE HEART DISEASE
UNIVERSITY OF NORTH CAROLINA
CHAPEL HILL, NORTH CAROLINA

DESCRIPTION (Adapted from Applicant's Abstract):
We propose to investigate the relationship of cognitive factors, specially pessimistic attributional style, to cardiovascular and neuroendocrine reactivity at rest, in response to and during recovery from laboratory and natural life stressors. A bi-racial sample of 80 postmenopausal women (age 40-69) and 40 aged-matched men will be recruited to participate. Blood pressure and its hemodynamic components (stroke volume, total peripheral resistance) will be measured during a laboratory protocol consisting of resting baseline, three stressor tasks (speech, mental arithmetic, and cold pressor ice tasks) and recovery periods. Plasma catecholamines and cortisol will also be measured at baseline and during stressors. The relationship of attributional style to blood pressure and neuroendocrine parameters will be assessed, controlling for variables quantifying demographic information and known risk factors for hypertension (socioeconomic status, parental history of hypertension). The association of attributional style with 24-hour ambulatory blood pressure and urinary cortisol measurements will also be assessed.

1F31MH012038-01
GROSSMAN, STACIE
GLUTAMATE RECEPTOR SUBUNITS AFTER SPINAL CORD CONTUSION
GEORGETOWN UNIVERSITY
WASHINGTON, D.C.

DESCRIPTION (adapted from applicant's abstract): Glutamate (GLU) is the major fast excitatory neurotransmitter of the central nervous system. Its effects are conveyed through ionotropic receptors that can be divided into two main classes: N-methyl-D-aspartate (NMDA) and non-NMDA. Each type of receptor is made up of any variety of a number of receptor subunits. Alterations in receptor subunits have been associated with a number of neurological disorders including Huntington's, Alzheimer's, and schizophrenia of this proposal is to gain a better understanding of EAA receptors in CNS trauma and neuronal degeneration that leads to cognitive and sensory-motor deficits. This can be done using an experimental neurodegenerative model of spinal cord injury. The overall aims of this

proposal are: (1) to examine the levels of ionotropic GLU receptor subunit expression following contusive spinal cord injury (SCI) compared to control levels; (2) to examine specific subpopulations of neurons and glia in the normal and injured spinal cord injury; 3) to examine phosphorylation status of receptor subunits after injury.

1F31MH012021-01
GUARINO, HONORIA
AIDS AND IDENTITY CONSTRUCTIONS
UNIVERSITY OF ARIZONA
TUCSON, ARIZONA

DESCRIPTION (Applicant's Abstract): The proposed research aims to provide the basis for the applicant's doctoral dissertation pursuant to the Ph.D. in Anthropology. By conducting extensive interviewing and participant-observation among people with HIV/AIDS in New York City, the applicant hopes to deepen her experience in the methodologies central to anthropology. In addition, the collection and analysis of a large corpus of linguistic data will enrich her skill in the technique of sociolinguistic analysis, as well as provide material for future publication. The research will also broaden her understanding of the social aspects of HIV/AIDS in the U.S. - a topical area that has been of interest to her throughout graduate school. Both the methodological and topical aspects of the research to be conducted during the fellowship year will prepare her for pursuing the practice of anthropology in an academic setting. The proposed research will investigate how the experience of having HIV/AIDS in the U.S. impact an individual's sense of personal and community identity and to what extent this identity is influenced by both verbal interactions in bureaucratic settings and dominant cultural discourses about AIDS. This project will employ the methods of cultural and linguistic anthropology, specifically participant-observation, interviewing and discourse analysis, to illuminate the ways in which people with AIDS' (PWAs') conceptualizations of self-identity are revealed in and constructed through their everyday speech, particularly narratives and conversation. A wide cross-section of PWA informants in New York City will be included in order to understand how experiences of HIV/AIDS are influenced by differences of race, class, gender, sexual orientation, and other factors. Strong basic research on PWAs' identity constructions and face-to-face verbal interactions within institutional structures, such as AIDS service organizations, will contribute to practical applications. Careful documentation of the needs of diverse groups of PWAs has the potential to facilitate better dialogue between bureaucrats and PWAs, leading to improved service for PWAs.

5F31MH011627-02
GUARRACI, FAY
MESOTELENCEPHALIC DOPAMINE SYSTEM AND LEARNED FEAR
UNIVERSITY OF VERMONT & ST AGRIC COLLEGE
BURLINGTON, VERMONT

DESCRIPTION (adapted from applicant's abstract): This project is designed to elucidate the role of the mesotelencephalic dopamine (DA) system in the expression of learned fear. Experiment 1 is an extension of preliminary results that found DA neurons in the ventral tegmental area (VTA) respond to conditioned fear stimuli in awake rabbits and is designed to specifically characterize the response patterns of VTA DA neurons which project to the amygdala central nucleus (ACe) and medial prefrontal cortex (mPFC) in response to conditioned fear stimuli. For additional confirmation that sites of

recorded neurons are located in the vicinity of dopaminergic neurons within the VTA, tyrosine hydroxylase-immunoreactivity will be used to identify the distribution of DA neurons. Experiments 2-4 are designed to determine the effects of DA activation in these two VTA DA terminal regions, on the expression of conditioned fear in rats. Experiment 2 is designed to determine if intra-ACe infusions of the D_1, agonist, SKF 82958, or the D_2 agonist, quinpirole, will alter the expression of conditioned fear. Experiment 3 is designed to determine whether intra-ACe infusions of the D_1 receptor antagonist, SCH 23390 or the D2 receptor antagonist sulpiride, will alter the expression of conditioned fear. If time permits, Experiment 4 will assess whether these drugs, infused into the mPFC, will alter the expression of conditioned fear. Together these experiments will provide important insight into the functional contribution of DA activation in the ACe and mPFC to fear behaviors.

5F30MH011041-04
GULANI, VIKAS
BRAIN FUNCTION IMAGING USING DIFFUSION WEIGHTED MRI
UNIVERSITY OF ILLINOIS
CHICAGO, ILLINOIS

DESCRIPTION (Adapted from applicant's abstract): The two most popular current methods for imaging brain function both rely on contrast changes that can be obtained from hemodynamic changes that occur during functional activation of a region of the brain. However, the blood flow changes that these methods utilize are secondary to the actual activation of neural tissue. The research proposed here will be aimed at developing a functional imaging technique that will allow the imaging of brain function without using flow phenomena. Rather, the study will make use of MRI's ability to measure water diffusion coefficients. It is known that the diffusion coefficient along white matter tracts and nerves is greater than that across these tracts. Protein configuration changes that occur when neurons are activated may cause this diffusion anisotropy to change. Thus, the ability to measure changes in diffusion anisotropy may allow the imaging of brain function as a much more fundamental level than is currently possible.
The study can be divided into three major parts, all of which will be developed concurrently. The first aspect of the work will consist of developing an alternative diffusion imaging sequence which allows the measurement of the diffusion tensor more rapidly than is currently possible. Second, the proposed method will be tested on frog sciatic nerves, which will be isolated and electrically activated within the magnet. It is hoped that diffusion anisotropy will be measurable upon electrical stimulation of these nerves. Lastly, an animal model for functional imaging will be developed using conventional techniques, and the new method for functional imaging will be tested on the animal model.

1F31MH012258-01
GUPTA, TARA
ALPHA 5 CONTAINING NEURONAL NICOTINIC RECEPTORS
GEORGETOWN UNIVERSITY
WASHINGTOM, D.C.

DESCRIPTION (Adapted from applicant's abstract): This project is designed to elucidate the role of the mesotelencephalic dopamine (DA) system in the expression of learned fear. Experiment 1 is an extension of preliminary results that found DA neurons in the ventral tegmental area (VTA) respond to conditioned fear stimuli in awake rabbits and is designed to specifically

characterize the response patterns of VTA DA neurons which project to the amygdala central nucleus (ACe) and medial prefrontal cortex (mPFC) in response to conditioned fear stimuli. For additional confirmation that sites of recorded neurons are located on the vicinity of dopaminergic neurons within the VTA, tyrosine hydroxylase-immunoreactivity will be used to identify the distribution of DA neurons. Experiments 2-4 are designed to determine the effects of DA activation in these two VTA DA terminal regions on the expression of conditioned fear in rats. Experiment 2 is designed to determine if intra-ACe infusions of the D1 agonist, SKF 82958, or the D2 agonist, quinpirole, will alter the expression of conditioned fear. Experiment 3 is designed to determine whether intra-ACe infusions of the D1 receptor agonist, SCH 23390 or the D2 receptor antagonist sulpiride, will alter the expression of conditioned fear. If time permits, Experiment 4 will assess whether these drugs, infused into the mPFC, will alter the expression of conditioned fear. Together these experiments will provide important insight into the functional contribution of DA activation in the ACe and mPFC to fear behaviors.

1F31MH011942-01
HAAS, STEPHEN
RELATIONAL MAINTENANCE OF COUPLES COPING WITH HIV/AIDS
OHIO STATE UNIVERSITY
COLUMBUS, OHIO

DESCRIPTION (Applicant's Abstract): During the next year, the candidate plans to continue to build his research skills in both qualitative methods in the dissertation work and quantitative methods through an ongoing research program with Dr. Brashers. One of the goals for this fellowship is to establish the groundwork for future research and interventions focused on helping couples to cope more successfully with a chronic illness such as HIV/AIDS. Relationship issues are central to persons' mental and physical health, and general quality of life. Because AIDS is becoming a chronic illness, quality of life research is as important as research that seeks to extend life. HIV/AIDS continues to affect the lives of an estimated 1 million persons in the United States and the millions of persons interconnected with those who have the virus. Research suggests that close friends and partners provide the majority of social support and informal care for persons living with HIV/AIDS (PLWHs). Studies have shown that access to social support is an important aspect of the PLWH's ability to reduce stress, anxiety, and depression which impacts physical health. Paradoxically, the relationships which provide the most support are placed under increased strain due to role redefinition, caregiver "overload," and lack of outside support due to social stigma. When persons assume the caregiving role, they often take on responsibilities that they are unprepared, ill-equipped, or unaccustomed to performing. Because maintaining support for the PLWH is so essential to both psychological and physical health, this study is designed to explore the strategies and routine behaviors that couples coping with HIV/AIDS use to provide support and maintain their relationship in the face of this chronic illness. Using a grounded theory approach, twenty-five adult couples (N=50) will be interviewed. Participant's responses will be analyzed to assess relationship maintenance behaviors.

5F31MH011560-02
HAENDEL, MELISSA
TRAPPING NOVEL GENES INVOLVED IN NEURAL DEVELOPMENT
UNIVERSITY OF WISCONSIN
MADISON, WISCONSIN

DESCRIPTION (Adapted from Applicant's Abstract):
The objective of the proposed research is to identify and ascertain the function of novel genes involved in nervous system development. To accomplish this, I have developed an in vitro cell culture system that will allow me to efficiently identify, mutagenize, and clone genes that are expressed in the embryonic nervous system. Briefly, embryonic stem (ES) cells are transfected with a gene trap vector and induced with retinoic acid to differentiate into neurons in vitro. The gene trap randomly inserts into the coding region of genes, thereby disrupting their function and allowing for expression of a lacZ reporter in cells that express the disrupted gene. Differentiated neurons derived from transfected ES cells are screened for expression of lacZ, as an indicator that a given ES cell clone harbors a disrupted neuronal gene. CDNAs of trapped genes expressed in neurons will be generated with lacZ-specific primers, cloned, and subjected to rigorous molecular characterization. Preliminary results from this screen have yield two ES cell clones that each contain a disrupted allele for a novel gene, both of which are expressed in the embryonic and neonatal nervous system of the mouse. These cells will be injected into host blastocysts in order to make germline chimeras. The normal function of these genes may be inferred from morphological defects of transgenic embryos homozygous for the gene trap allele.

5F31MH011816-02
HALL, CATHERINE
PROTEIN 14-3-3 FUNCTION IN LEARNING AND MEMORY
BAYLOR COLLEGE OF MEDICINE
HOUSTON, TEXAS

DESCRIPTION (Adapted from Applicant's Abstract):
To further understand mechanisms of the brain, research has focused on fundamental functions of the brain such as learning and memory. Recent discoveries have revealed that a member of the 14-3-3 family of proteins is involved in learning and memory processes. How 14-3-3 plays a role in these processes is poorly understood. Using learning and memory as a biological assay, 14-3-3 protein function may be revealed. This proposal is designed to characterize proteins which interact with 14-3-3 in learning and memory. The following specific aims are designed to further test the hypothesis that 14-3-3 protein function is essential for learning and memory processes. 1) Identify proteins that interact with 14-3-3. Four Drosophila cDNA clones encoding proteins that interact with 14-3-3 in the yeast two-hybrid system will be sequenced and the interactions of their products with 14-3-3 confirmed by in vitro binding assays and coimmunoprecipitation in yeast and in vivo. 2) Elucidate the expression patterns of 14-3-3 interacting proteins within the brain mRNA and protein expression of 14-3-3 interacting cDNA clones will be determined using Northern analysis, in situ hybridization and immunohistochemistry. 3) Determine the phenotypes of mutants of 14-3-3 interacting proteins. Flies carrying mutations in 14-3-3 interacting protein genes will be tested for deficits in learning and memory using classical olfactory conditioning paradigms.

1F30MH012305-01
HALTERMAN, MARC

SENSING HYPOXIA IN THE CNS USING HERPES VECTORS
UNIVERSITY OF ROCHESTER
ROCHESTER, NEW YORK

DESCRIPTION: (Applicant's abstract) Ischemic damage to the brain results in substantial morbidity during the perinatal period as well as mortality in the later decades of life. Studies in the intact animal as ell as in vitro have established that the extreme physiologic perturbations which occur during CSN ischemia trigger a delayed form of neuronal death which is dependent on new gene transcription and that hypoxia triggered gene responses precede activatio of delayed apoptotic cell death. One approach to the identification of novel therapeutic strategies which would protect against this form of neuronal cell death is through examination of the mechanisms which direct hypoxia responsive gene expression in the CNS. The phylogenetically conserved hypoxia response is manifest in the mammalian systems through transcriptional activation and post-transcriptional mRNA stabilization. In the periphery, transcriptional events are known to be mediated through the hypoxia inducible transcription factor, HIF-1alpha, which binds cognate cis elements in the promoter region of a restricted set of genes thereby simulating the rate of gene transcription. Information regarding the utilization of this hypoxia responsive mechanism within the various cellular compartments of the CNS (neuronal, astrocytic and microglial) and their relationship to apoptotic neuronal loss is lacking, however. Broadly, we hypothesize that early in the post-ischemic CNS hypoxic-regulated gene expression exhibits heterogeneity within the cellular compartments in the CNS and that this response triggers a sequence which eithe directly or indirectly elicits delayed neuronal death. We plan to exploit hypoxia responsive HSV viral vectors to map the regional and temporal evolutio of hypoxic signaling within the compartments of the ischemic murine CNS. Subsequent studies will utilize HIF neuronal isoform specific antibodies to characterize HIF isoform induction, cellular localization and confirm DNA binding reactivity through EMSA supershift assays all under hypoxic conditions We hypothesize that these experiments will characterize heterogeneous hypoxic response and will define discrete factors in ischemia induced CNS transcriptional activation. Our long-term goals are to identify early response in the ischemic brain and subsequently identify regulatory nodes in the hypoxi signal cascade which ca selectively modulate hypoxia gene activation. Such findings will highlight novel therapeutic strategies directed against hypoxia induced delayed neuronal death.

1F31MH011686-01A1
HAN, TINA
SEXUAL DIFFERENTIATION OF VASOPRESSIN EXPRESSION
UNIVERSITY OF MASSACHUSETTS
AMHERST, MASSACHESETTS

DESCRIPTION (Adapted from applicant's abstract): The sexually dimorphic vasopressin system of the rat may serve as an informative in vivo model for elucidating the cellular and molecular mechanisms controlling neuronal development. Male rats possess two to three times the number of vasopressin neurons than do females in the bed nucleus of the stria terminalis and the medial amygdala (BST/MA). Gonadal steroid hormone levels during a perinatal period determine the number of vasopressineric neurons in adulthood in these areas. This proposal first aims to clarify whether or not galanin-only production is a "default" phenotype to vasopressin and galanin coexpression. I will do this by developing a cell birth profile for galaninergic neurons

and comparing this profile with that generated for vasopressinergic neurons (Specific Aim 1). Secondly, using in situ hybridization for vasopressin and galanin mRNA, I will determine which steroid hormone is critical in the sexual differentiation of this system (Specific Aims 2 and 3). Finally, I will use differential display polymerase chain reaction (ddPCR) to isolate genes in the BST/MA that may be part of a steroid-regulated pathway that initiates vasopressin production (Specific Aim 4). These studies will not only contribute to the understanding of how steroid hormones affect neural and behavioral development, they may succeed in identifying molecular components involved in steroid-dependent neuropeptide expression.

1F31MH012216-01
HARLEM, ANDREW
CULTURE THEORY AND MENTAL HEALTH IN CLINICAL PSYCHOLOGY
UNIVERSITY OF CHICAGO
CHICAGO, ILLINOIS

DESCRIPTION (Applicant's Abstract): The proposed research will investigate the extent to which recent advances in the understanding of cultural diversity in psychological processes are being integrated into the practice of clinical psychology and the training of clinical psychologist in the United States. Specific aims of the research are to (I) assess the state of expert clinical knowledge regarding the influence of socio-cultural factors on cognitive affective and somatic aspects of the person and on "personhood" itself (2) describe and critique the conceptual models of culture race and ethnicity that inform current multicultural approaches in mental health research and practice and (3) illuminate the implicit theories used by psychologists to resolve apparent tensions between respect for individual experience, cultural) difference and universal psychological processes. The project will employ a qualitative, ethnographic interpretive research paradigm based on the methods of cultural psychology. Data will be collected during structured interviews with 40 clinical psychologists and from 50 multicultural curricula of clinical psychology graduate programs around the country. The interview data will undergo rigorous content analysis in order to provide insight into how clinica psychologists are responding to the call far responsive and meaningful treatment among a population that is increasingly diverse as well as increasingly committed to maintaining traditional cultural understandings lifestyles and identities. Through this contribution to the literature on culture and mental health. the project endeavors to son out the heterogeneous set of multicultural agendas that abound in professional discourse in the hope that clarity can produce purpose. old debates can be transcended and social science can continue to contribute to the quality of mental health services available during the coming decades. The project will also have implications for the study of social and group processes. Research-clinical dialogue, and theories relating collective meaning to individual experience.

5F30MH011587-02
HARRIS, ELANA
PROPERTIES AND CONNECTIONS OF ENTORHINAL NEURONS
HEALTH SCIENCE CENTER AT BROOKLYN
NEW YORK, NEW YORK

DESCRIPTION (Adapted from Applicant's Abstract):
Neurons of the entorhinal cortex are at the intersection of two neuronal circuits, a "locational" circuit comprised of entorhinal and hippocampal neurons, and a "directional" circuit which includes

entorhinal and other retrohippocampal neurons. The goal of this project is to examine properties of deep layer entorhinal neurons and their connectivity with elements of both the directional and locational circuits. Specifically, we will focus on the inputs from subiculum and presubiculum to deep layer medical entorhinal neuronsin rat brain slices. Fundamental data needs to be acquired: 1) cell shape and dendritic extent; 2) basic membrane properties; 3) target neurons of the two inputs; 4) functional nature of each input (i.e. excitatory or inhibitory); and 5) possible convergence of subicular and presubicular inputs into single entorhinal neurons. Perhaps surprisingly, these studies have not been done. Intracellular recording techniques in brain slices will be used t acquire these data. The techniques are well established in the sponsor's laboratory. The project is straightforward for training in the sense that the data are not difficult to obtain. However, since it is a project intended to collect some of the most basic information about a brain region, there is considerable latitude to focus experimental emphasis on a particular discovery made along the way.

1F32MH011849-01A2
HAZELTINE, RICHARD
NEURAL BASIS OF RESPONSE SELECTION
STANFORD UNIVERSITY
STANFORD, CALIFORNIA

DESCRIPTION (Applicant's abstract): This project will investigate the neural basis of response selection using functional magnetic imaging (fMRI). Functional imaging is playing an increasingly significant role in cognitive neuroscience research, including the topics of memory, vision and motor control. The proposed experiments are an attempt to integrate behavioral and imaging findings in these three areas using a paradigm called the flanker task The flanker task has been shown behaviorally to evoke response selection processes for stimuli that do not elicit an overt response. A procedure is developed to isolate the neural loci of these selection processes and to examine their sensitivity to stimulus properties. With this new method, a new understanding of the interaction between selective attention and response competition can be created.

1F31MH011941-01A1
HERNANDEZ, MARIA
HIV/AIDS PREVENTION IN WOMEN--TRAINING IN BIOSTATISTICS
UNIVERSITY OF PUERTO RICO RIO PIEDRAS
RIO PIEDRAS, PUERTO RICO

DESCRIPTION (Applicant's Abstract): This 3-year predoctoral request comes from a candidate who proposes to develop her research skills in biostatistics and to carry out research in the HIV/AIDS prevention area. Women become one of the most HIV/AIDS "at risk groups" as every day goes by. Puerto Rico has one of the highest incidence rates of HIV/AIDS in the world. The objective of the research component of this proposal is to revise and evaluate an intervention for HIV/AIDS prevention undertaken with 240 young sexually active heterosexual Puerto Rican women in the San Juan Metropolitan Area. This proposal will focus on: 1) evaluating the recruitment/retention strategy used in the intervention, 2) analyzing the effectiveness of random assignment, 3) evaluating short term effects of the intervention study, 4) developing data analysis that relates important variables, 5) developing a data analysis plan comparing the intervention results with a similar

community based prevention project, and 6) revising and validating three instruments that were used in the intervention study. This will include: 1) evaluation of the recruitment and retention strategy (R&R) using: a) data obtained from a systematic assistance register, b) two Strategy Effectiveness Questionnaires (SEQ) and c) Structured Open-Ended Interviews (SOI); 2) analysis of random assignment focusing on participants assigned to the two conditions on the basis of demographic variables and on the dependent measures; 3) implementing the intervention with one experimental group of 120 women and one control group of same size (procedures for statistical data analysis will be performed for intervention impact evaluation purposes); 4) correlational and multiple regression analyses to relate important dependent and sociodemographic variables; 5) comparative analyses between intervention outcomes and data from another community project; and 6) validating the Diverse Emotional States Scale (DESS), the Self-efficacy Scale (SES), the Power Differential Scale (PDS), and the Social Support Questionnaire with a sample of 240 women who will participate in the intervention.

5F31MH011712-02
HOFFMAN, DAX
VOLTAGE GATED K+ CHANNELS FROM CA1 PYRAMIDAL NEURONS
BAYLOR COLLEGE OF MEDICINE
HOUSTON, TEXAS

DESCRIPTION (Adapted from applicant's abstract): As voltage-gated potassium channels are the primary regulators of membrane excitability, the types and distributions present on a neuron's dendrites will effect how signals are conveyed through it's dendrites. Recent technological advances have made it possible to record single-channels from dendrites. The biophysical and pharmacological characterization of three classed of voltage-gated potassium channels in the soma and dendrites of hippocampal CA1 pyramidal neurons is proposed. Both macroscopic and single-channel properties, along with estimates of channel density will be described for each of the three classes of channels under proposed study: the transient, A-type channel, the delayed-rectifier type, and the large conductance, calcium-activated type. The information gathered here will not only increase our knowledge of voltage-gated potassium channels and their role in dendrite physiology but may also contribute to our understanding of the initiation of epileptiform activity and of memory-loss related diseases.

5F31MH011530-03
HOLROYD, CLAY
COGNITIVE AND NEURAL ASPECTS OF HUMAN ERROR PROCESSING
UNIVERSITY OF ILLINOIS AT CHICAGO
CHICAGO, ILLINOIS

DESCRIPTION (Adapted from Applicant's Abstract):
Many higher order cognitive functions that plan, regulate, and monitor behavior have been neglected by the community of cognitive psychologists. We intend to address this shortcoming by determining the behavioral nature and neural implementation of one such function, which we call error processing, in humans. It has been demonstrated that activation of an error detection system manifests itself at the scalp as a negative deflection in the event-related brain potential (ERP). Preliminary evidence suggested that this error-detection system is mediated, at least in part, by the anterior cingulate gyrus. The primary goal now is to confirm that error-related activity occurs in the anterior cingulate by

employing functional neuroimaging techniques such as ERPs and magnetoencephalograms (MEG), and by the development of a biologically plausible computational model of anterior cingulate dynamics. A secondary goal is to distinguish, using ERPs, between behaviors that activate and behaviors that do not activate the error detection system. This research is expected to elucidate the nature of several clinical disorders, including Obsessive-Compulsive Disorder and various psychopathologies associated with lesions of the frontal lobes.

1F32MH012300-01
HORIUCHI, JUNJIRO
CREB PHOSPHORYLATION AND LONG TERM MEMORY IN DROSOPHILA
COLD SPRING HARBOR LABORATORY
COLD SPRING HABOR, MAINE

DESCRIPTION (Adapted from Applicant's Abstract):
The transcription factor, CREB (cAMP response element binding protein), controls the expression of various genes in response to cAMP and calcium levels. It is regulated post-translationally by phosphorylation. Most interestingly, CREB is important for the formation of long-term memories (LTM) in many organisms, including mammals. In Drosophila melanogaster, overexpressing an activator form of CREB enhances the formation of LTM such that fewer trainings are required for flies to remember an associative task. Overexpressing a repressor form of CREB reduces the formation of LTM such that flies do not remember an associative task after the usual number of trainings.
We are interested in studying the regulation of CREB and the effects that this regulation has on LTM formation. Phosphorylation site mutations in CREB will be made and assayed for changes in transcriptional activity in tissue culture cells and LTM formation in flies. Also, specific brain regions where CREB activity is required for the formation of LTM will be identified by overexpressing CREB only in specific areas of Drosophila brains. Finally, the phosphorylation state of a specific site, shown to be critical for CREB activity, will be studied during the formation of LTM.
These studies will help elucidate the mechanisms of CREB regulation and will be important in the studies of both signal transduction pathways and research in memory formation.

1F31MH012232-01
HOUSTON, DEREK
TALKER VARIABILITY AND EARLY WORD REPRESENTATIONS
JOHNS HOPKINS UNIVERSITY
BALTIMORE, MARYLAND

DESCRIPTION (Applicant's abstract): Recent research in infant speech perception indicates that infants learn a great deal about the sound organization of their language during the first year of life and that they use this information as a indicator of the syntactic organization of the language. Current diagnostic methods for identifying Specific Language Impairments (SLI) are only applicable with children 3 to 4 years of age. A better demarcation of the critical linguistic landmarks during the period between 6- and 18-months of age will help in developing diagnostic tools for SLI that can be used at a much earlier developmental stage. These experiments will investigate the conditions in which infants form representations of words that are generalizable across different voices. Infants will be familiarized with works presented with one or several voices and then tested on their

recognition of these words presented in a different voice by examining their orientation times to passages containing the familiarized words compared to passages that do not. The first part of the project will investigate how well infants can generalize words across specific voice-property differences (i.e., voice gender, average pitch, pitch contour). In Part Two infants are familiarized with words using several voices to explore the possibility that word representations might be more or less robust and generalizable when formed with multiple talkers than with a single talker. Part Three investigates the possibility that experience with a talker's voice improves infants' ability to analyze and encode the speech from that talker. Specifically, infants will be pre-exposed to the voice that will present the passages before the familiarization phase to see if word recognition performance is improved.

5F30MH011169-04
HYMEL, ERNEST
MODELED PHOTORECEPTOR TO HORIZONTAL CELL INTERACTIONS
UNIVERSITY OF TEXAS MEDICAL BR
GALVESTON, TEXAS

DESCRIPTION (Adapted from applicant's abstract): A mathematical model of the photoreceptor that includes the biochemical and ion conduction processes that convert light into electrical energy has been developed using data from the literature. A series of experiments has been designed to obtain data for a complete kinetic analysis of all the known ligand- and voltage-gated ion channels of the cone horizontal cell. These experiments consist of using frequency domain admittance analysis of pharmacologically isolated ion channels. These data will be incorporated into a mathematical model of a cone horizontal cell which will then be coupled via a model synapse to the photo-receptor model. As in the case of the photoreceptor model, the model synapse will be based on data and similar models available in the literature. This coupled cell model will be used to describe the process of light transduction into electrical energy and the transmission process between photoreceptor and horizontal cell.

5F30MH011272-02
IRWIN, SCOTT
EXPRESSION AND FUNCTION OF FMRP DURING DEVELOPMENT
UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN
CHAMPAIGN, ILLINOIS

DESCRIPTION (Adapted from Applicant's Abstract):
Our laboratory has recently obtained evidence from an in vitro synaptoneurosome preparation that the fragile X gene product, a protein termed FMRP, is translated from mRNA at locations near synapses in response to glutamatergic activation of metabotropic receptors. This finding complements other work on the fragile X gene (FMR-1) and the fragile X syndrome, a form of mental retardation correlated with the absence of normal FMRP expression, all of which suggest that FMRP may play a role in the process whereby synaptic activity during development and/or learning results in a structural and functional maturation of the synapse. We propose a series of basic studies of the rodent brain designed to further explore in vivo, 1) the spatio-temporal pattern of the expression of FMRP during development, 2) the possible correlation of FMRP expression with other major developmental processes, such as synaptogenesis, in order to explore possible reasons for the pathological effects of FMRP deficiencies on brain development, and 3) the effects of behavioral

experience on FMRP expression in brain regions known to exhibit structural plasticity in response to behavioral experience manipulations, studying visual cortex in monocularly deprived animals and animals exposed to an enriched environment, and motor cortex in animals after acrobatic motor skill learning. Fragile X syndrome, which can arise from a mutation that prevents gene expression or from point mutations affecting the structure of the gene product, is one of the most common forms of inherited mental retardation known. Furthermore, it is commonly associated with autism and attention deficit hyperactivity disorder. Knowledge of the role of FMRP in synapse maturation and brain function may well give rise to treatments for these syndromes.

5F32MH011729-02
IVKOVICH, DRAGANA
ONTOGENY OF TRACE CONDITIONING IN ANIMALS AND HUMANS
NATIONAL HEALTH & ENVIRO EFFECTS RES LAB
RESEARCH TRIANGLE, NORTH CAROLINA

DESCRIPTION (Adapted from applicant's abstract): Classical eye blink conditioning has become a powerful preparation for studying the neural bases of learning and memory in both animals and humans. A well-defined neural circuit involving the cerebellum and brainstem is sufficient to support simple associative learning, i.e., delay conditioning. However, more complex forms of learning, such as trace conditioning, appear to involve forebrain systems involved in cognition, i.e., the hippocampus. Because the cerebellum and hippocampus develop postnatally in most mammals, eye blink conditioning may be an idea model for studying the role of these structures in cognitive development.
The main goal of this proposal is to use classical eye blink conditioning to study early neurocognitive development in rats and humans. Comparative studies of the development of eye blink conditioning will characterize the ontogeny of delay and trace eye blink conditioning in both species. The studies are designed to test the hypothesis that trace conditioning will emerge later than delay conditioning, and that the ontogeny of trace conditioning is dependent on maturation of the hippocampal cholinergic system and its interactions with the cerebellum. Cross-sectional and longitudinal behavioral studies in rat pups at different ages will be used to determine the age at which pups are capable of forming the associations underlying trace and delay conditioning, versus the age at which these forms of learning come to be expressed. The proposed studies will also determine the effects of disrupting normal hippocampal development on the emergence of delay and trace conditioning. Finally, the ontogeny of delay and trace conditioning in healthy full-term infants will be determined as a prelude to future studies of populations of infants at high risk for neurological damage of various etiologies.

5F31MH011773-02
JACOBSON, C JEFFREY, JR
DREAMS, VISIONS, AND PERSON IN A PUERTO RICAN BARRIO
CASE WESTERN RESERVE UNIVERSITY
CLEVELAND, OHIO

DESCRIPTION (Applicant's Abstract): This anthropological study, examines dream, visionary, and hallucinatory phenomena and their role in cultural understandings of personhood and identify among lower and working class Puerto Ricans in a U.S. inner-city context. Combining ethnographic methods and structured psychiatric questionnaires, the study will describe how diverse

experiences of remarkable mental, emotional, and somatic imagery influence personal and social identity. In phase I, a community-level, ethnographic description of a inner-city, Puerto Rican Barrio will combine systematic interviewing and participant observation with data from the US Census and local health statistics. Interviews will focus on interpersonal relations and on the experience and sharing of diverse psychological and spiritual phenomena including emotions, memories, dreams, and visions. This ethnopsychological ethnography will provide context for a more focused examination of the experience and meaning of visions. In phase II, 50-60 individuals will to discuss and evaluate their own and other s dreams, visions, and hallucinations will be interviewed. In addition, structured psychiatric questionnaires probing diagnoses and symptoms will be administered. As a meaning centered description of personhood and visionary experience among inner-city Puerto Ricans, the study will provide a culturally valid basis for evaluating and comparing the folk-spiritual and professional-psychiatric significance of visionary experience.

5F31MH010957-03
JACOBY, ROY
INPUTS TO PARASOL GANGLION CELLS IN MACAQUE RETINA
UNIVERSITY OF TEXAS HLTH SCI CTR
HOUSTON, TEXAS

DESCRIPTION (Adapted from Applicant's Abstract):
This research will describe the synaptic input to parasol ganglion cells in the primate retina. These cells provide the major input to the magnocellular layers of the lateral geniculate nucleus, which in turn provide input to cortical areas that mediate the perception of movement in the visual field. Peripheral parasol cells receive 80% of their input from amacrine cells and the remainder from bipolar cells, but the specific types of presynaptic amacrine cells and bipolar cells are not known. My working hypothesis is that two subtypes of diffuse bipolar cell provide the primary input, one to each of the two subtypes of parasol cells. I will also test the hypothesis that two kinds of narrowly-stratifying, wide-field amacrine cells receive input from the same bipolar cells and also make synapses onto parasol cells. First, tissue containing intracellularly-injected parasol cells will be immunolabelled and analyzed using a confocal microscope to determine whether various types of bipolar cells and amacrine cells make appositions onto their dendrites. Neurons that appear to be presynaptic to parasol cells will then be studied in the electron microscope to determine whether the close appositions seen at the light microscopic level represent areas of synaptic contact. One approach to identifying the presynaptic cells will be to reconstruct serial tangential sections through the injected parasol cell dendrites, and the other will be to modify the double-labelling techniques for electron microscopy.

5F30MH011331-03
JASPAN, HEATHER
CD4, CD8 AND VIRAL MRNA IN HIV POSITIVE INFANTS
TULANE UNIVERSITY OF LOUISIANA
NEW ORLEANS, LOUISIANA

DESCRIPTION (Applicant's abstract): This predoctoral M.D.-Ph.D. fellowship requesting 5 years of support, comes from Heather Jaspan at Tulane Medical School. The applicant evaluates current methods of assessing the progression of those infected with human immunodeficiency virus (HIV) as being limited,

lacking accuracy, and requiring a large number of cells. These problems are especially disadvantageous to the pediatric population for whom only a small number of cells is available. The applicant proposes to use the molecular technique - Quantitative Competitive Reverse Transcriptase Polymerase Chain Reaction (QC-RT-PCR) for quantification of CD4 and CD8 mRNA in Peripheral Blood Mononuclear Cells (PBMCs). This method is more accurate and requires fewer cells. The correlation between amount of these mRNAs and number of cells (determined by flow cytometry) will then be calculated, and the applicant will determine if and how this correlation is different in HIV infected individuals. The applicant will further this technique for measurement of viral load using QC-RT-PCR of Gag Nef, and Vpu mRNAs of HIV will also be quantitated to see their relationship to CD4-cell counts. The applicant will be concentrating on vertically infected babies for whom AIDS pathogenesis and progression has not yet been clearly defined. Therefore, the use of the applicant's molecular technique to measure CD4, CD8 and viral protein mRNAs aims to more clearly define progression of HIV disease in the pediatric population which will be important for prognosis and ultimately for treatment.

1F32MH012067-01
JIN, XIAOWEI
MOLECULAR MECHANISMS OF CIRCADIAN ACTION OF MELATONIN
MASSACHUSETTS GENERAL HOSPITAL
BOSTON, MASSACHUSETTS

DESCRIPTION (Adapted from applicant's abstract): The pineal hormone melatonin elicits potent circadian and reproductive effects in mammals through high-affinity guanine nucleotide binding protein (G protein)-coupled receptors. Two melatonin receptor subtypes have been cloned from mammals and designated Mel1a and Mel1b receptors. A biological clock in the suprachiasmatic nuclei (SCN) is responsible for generating and controlling the melatonin rhythm in mammals. Melatonin elicits two distinct actions in the SCN, the acute inhibition of neuronal activity and phase shifting. Both Mel1a and Mel1b gene expressions have been found in the SCN. Targeted disruption of the Mel1a receptor only eliminates the acute inhibitory effect of melatonin on neuronal firing, yet the melatonin-mediated phase shifts are only modestly altered in the Mel1a receptor-deficient mice. Because pertussis toxin still blocks melatonin-induced phase shifts in the Mel1a knockout mice, and the only known receptor subtype expressed in the SCN of Mel1a receptor-deficient mice is the Mel1b receptor, we hypothesize that both Mel1a and Mel1b are involved in mediating the effect of melatonin in the SCN. We have cloned the mouse Mel1b receptor gene, and the generation of Mel1b knockout mice is also underway. Here we propose to characterize the mouse Mel1b receptor pharmacologically and functionally. We also plan to perform electrophysiology and behavior studies with the Mel1b knockout and Mel1a/Mel1b double knockout mice. Our studies will provide valuable insight into the molecular mechanisms underlying the circadian action of melatonin in the mammalian SCN.

1F31MH012081-01
JOHNS, LAURA
CHROMAFFIN GRANULE MOVEMENT NEAR THE PLASMA MEMBRANE
UNIVERSITY OF MICHIGAN
ANN ARBOR, MICHIGAN

DESCRIPTION (Adapted from applicant's abstract): Although much is known about exocytosis in chromaffin cells, little is known about secretory

granule movement close to the plasma membrane preceding the final fusion event. A key aspect of the proposal is our ability to visualize chromaffin granules in real time. A fusion protein of atrial natriuretic peptide and green fluorescent protein that is expressed by transient transfection is sorted to chromaffin granules. Using the optical technique of total internal reflection, we can visualize fluorescent chromaffin granules in living cells that are localized within 1-2 granule diameters of the plasma membrane. I hypothesize that movement and placement of chromaffin granules close to the plasma membrane are highly regulated processes that help define the availability of granules to undergo exocytosis. The focus of this proposal is to determine whether cofactors and proteins known to influence the final secretory response act at least in part by controlling these prefusion events. My specific aims are the following: (1) to determine the location and movement of chromaffin granules close to the plasma membrane under basal and secretory conditions, (2) to determine the relationship between the known effects of ATP and Ca2+ on granule priming before secretion and granule movement adjacent to the plasma membrane and (3) to determine the role of SNAREs and Rab3a, specific proteins of the secretory pathway in granule movement and placement adjacent to the plasma membrane.

1F31MH012165-01
JOHNSON, JENNIE
MULTIELECTRODE NEUROPHYSIOLOGY OF ATTENTION
NEW YORK UNIVERSITY MEDICAL CENTER
NEW YORK, NEW YORK

DESCRIPTION (Adapted from applicant's abstract): This application proposes to examine the spatio-temporal organization of the neurophysiology of attention using multisite, multiple microelectrode recordings in a novel rat model of selective attention. The first set of experiments will determine the role that coherent, gamma band oscillations within and between primary sensory cortices play in attending to single or combinations of sensory events. The second set of experiments will determine the physiological mechanism(s) whereby an attention-enhancing drug improves behavioral performance. The hypothesis to be tested is that coherence in the neuronal firing in the gamma band frequency range across cortical sites is an underlying substrate of selective attention.

1F31MH012213-01
JONES, LAURA
DEVELOPMENT OF EFFORTFUL CONTROL
UNIVERSITY OF OREGON
EUGENE, OREGON

DESCRIPTION (Adapted from applicant's abstract): The objectives of this project are to trace the development of effortful control between the ages of 37 and 48 months, and to investigate children's verbal and physical self-regulatory strategies for control during this period. Effortful control is a major contributor to the development of conscience and the control of emotion for both children and adults. Three elements of executive control include: (1) conflict resolution, (2) the ability to monitor errors and (3) modulation of behavior to meet situational demands. Two proposed cross-sectional studies would provide a fine-grained analysis of the relationship among these components of executive control The first would use a modified Simon-Says task to induce conflict, and then examine the development of children's inhibitory control, strategies for control, and error detection. A second study would introduce randomly mixed conflict

and non-conflict trials to examine the development of these functions and explore whether they function independently at each of the ages studied. Both studies would use the Children's Behavior Questionnaire (CBQ), a caregiver report of temperament, to examine the relationship between children's capacity for conflict resolution, error detection and strategy use in the laboratory, and caregiver report of children's levels of effortful control and negative affect in naturalistic settings.

5F30MH011394-02
KAPADIA, MITESH
NEURONAL BASIS OF PERCEPTUAL LEARNING
UNIVERSITY OF PENNSYLVANIA
PHILADELPHIA, PENNSYLVANIA

DESCRIPTION (Adapted from Applicant's Abstract):
Although the term "learning" is normally applied to the storage of complex percepts, such as the recognition of new objects or faces, there is increasing evidence that our perception of even simple stimulus attributes, such as the orientation or position of a line, is not fixed but can improve considerably with practice. These improvements have been termed perceptual learning to emphasize the similarities between these processes and classical forms of learning in other parts of the brain. This study examines learning in early levels of visual processing, utilizing the visual system to examine basic mechanisms of neuronal plasticity.
A combination of approaches utilizing extracellular recording, optical imaging and pharmacologic manipulations will be used to examine perceptual learning in a visual discrimination task and the neuronal substrate by which This process takes place. Studies in somatosensory and auditory systems have shown that perceptual improvements in sensory discriminations are correlated with changes in neuronal response specificity at early levels of cortical processing. There is an increase in the amount of cortex which responds to the discrimination stimulus, which presumably leads to improved perceptual capabilities by allowing a larger number of neurons to participate in the task.
We seek to observe analogous changes in the visual system by obtaining maps of the functional architecture of primary visual cortex before and after monkeys are trained on a visual discrimination for a period of several months. Through a subsequent series of pharmacologic manipulations in which we block various inputs to the region of cortex in which these changes occur, we hope to elucidate the patterns of neuronal connectivity which form the substrate for the perceptual improvements.

1F30MH012157-01
KEENE, CHRISTOPHER
TRANSPLANTATION OF FETAL LGE IN HUNTINGTONS MODELS
UNIVERSITY OF MINNESOTA TWIN CITIES
MINNEAPOLIS, MINNESOTA

DESCRIPTION (Adapted from applicant's abstract): The ultimate objective of the proposed research is to provide clinicians with data and techniques requisite for the implementation of transplantation of human fetal neural tissue in the treatment of Huntington's Disease (HD). Specific Aim 1 will address whether human fetal LGE (hfLGE) can ameliorate the cognitive deficits associated with HD. We will assess this using delayed alternation

and spatial learning and memory tests pre- and post-transplantation in a rat model of HD. These measures will be correlated with graft growth, survival, and the neurochemical phenotype of the grafts to identify graft characteristics which are important for recovery of cognitive function. hfLGE transplant efficacy must be assessed in an animal model evolutionarily more closely related to humans in order to test more complex behavioral measures and to evaluate the clinical applicability of the procedure. Specific Aim 2 addresses these issues in a non-human primate model of HD. hfLGE will be transplanted into rhesus monkeys with 3-nitropropionic acid lesions of the caudate and putamen. Monkeys will be tested behaviorlly pre- and post-transplantation by videotape assessment of incidence of choreiform movements, orofacial dyskinesia, dystonia, and manual dexterity. Further tests will be conducted to assess cognitive effects, including passive avoidance and visual discrimination tasks. At the end of the behavioral testing the animals will be sacrificed and their brains removed for histological processing. Growth and survival of the graft, as well as its cellular phenotype, will be correlated with behavioral data to evaluate graft efficacy and potential for clinical application. Clinically, one of the most important weaknesses of neural cell transplantation procedures is the absence of a reliable method for monitoring graft development. In Specific Aim 3, fetal neural tissue grafts in rats and monkeys with excitotoxic striatal lesions will be monitored using 1-H nuclear magnetic resonance spectroscopy (NMRS) which utilizes MEGA, a frequency selective refocusing technique, to monitor GABA levels in vivo. In simultaneous experiments, rats and monkeys with intrastriatal lesions and grafts will be monitored using NMRS. The striata of rats will be imaged/measured using the 9.4 Tesla magnet pre- and post-lesioning. Volumetric, morphologic and immunohistochemical measures will be taken periodically and correlated with the values obtained from the imaging studies and with behavioral measures from each rat. The non-human primate studies will utilize the same animals from Specific Aim 2. The imaging data will be correlated with the final histological and behavioral measures obtained from the primate subjects at the end of the experiments to evaluate the clinical efficacy and applicability of this NRMS technique in human fetal tissue transplantation.

1F31MH011758-01A1
KELLER, JENNIFER
PROCESSING DEFICITS IN PSYCHOPATHOLOGY
UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN
CHAMPAIGN, ILLINOIS

DESCRIPTION (Adapted from applicant's abstract): Inherent in the criteria for many of the disorders in DSM-IV (American Psychiatric Association, 1994) are cognitive impairments, such as attentional and language dysfunctions. The proposed research will examine five hypotheses about potential common and differential deficits in schizophrenia and depression related to working memory and sustained attention. Cognitive differences between schizophrenics and depressives will be assessed by examining ERP component latency and amplitude, as well as accuracy and recall performance. ERP data will be obtained as responses to target and nontarget tones in Experiment 1 and to sentences in which the terminal words are either semantically congruent or incongruent with the text preceding it in Experiment 2. Both experiments rely on well researched phenomena and measures in the normative cognitive psychophysiology literature and on specific procedures developed in the applicant's laboratory. Both experiments have been successfully piloted with inpatient volunteers.

5F32MH011892-02
KELLY, ROSEMARY
MENTAL ILLNESS IN PREGNANCY AND RISK OF POOR OUTCOME
UNIVERSITY OF CALIFORNIA
DAVIS, CALIFORNIA

DESCRIPTION (Adapted from Applicant's Abstract):
Few population-baed investigations have been previously undertaken that examine the association between psychiatric disorders in pregnancy and poor pregnacy outcome. In the past decade, case control studies suggest that schizophrenia is assoicated with decrease prenatal care and poor pregnacy coutcome, but the results have been contradictory. Furthermore, it has been found that 10-20% of pregnant women abuse sustances. The long term consequences of untrated maternal psychiatric illness are potentially grave as the cognitive ans emottional health of the infant are affected. This study will begin to address the gaps in our knowledge of the epidemiology, course and outcome of psychiatric disordes in pregnancy. The soecific aims of this investigation are to:1) examine the rates of psychiatric and substance abuse diagnoses and their comorbidity at the time of delivery as recorded on hospital discharge summary 2) examine the soci-demographic characteristics of the mothers with psychiatric and substance abuse diagnoses at delivery 3) measure the association between maternal psyhiatric diagnoisis and selected poor maternal and fetal outcomes and length of hospital stay. We will conduct a cross sectional epidemiologic study using the California Health Infornmation for Policy Project (CHIPP) data set, which contains material and discharge and birth certificate data for the approximately 600,000 births in California in 1992. Logistic regression models will be used to test for significant associations between demograghic variables and psychiatric diagmoses, as well as psychiatric dignoses and poor pregnancy outsomes while examining the effects of demographic, maternal hypertension and diabetes, parity, and prenatal care.

7F30MH010915-05
KESARI, SANTOSH
HERPES VIRUS THERAPY FOR EXPERIMENTAL BRAIN TUMORS
UNIVERSITY OF PENNSYLVANIA
PHILADELPHIA, PENNSYLVANIA

DESCRIPTION (Adapted from Applicant's Abstract): This predoctoral (Pre-M.D.-Ph.D., F30) requests 4 years and 10 months of support for training in molecular biology and neurobiology. The ultimate goal of the research project within this training program is to screen and select viruses that have potential as therapeutic agents for the treatment of patients with primary brain tumors, and to expand the spectrum of potentially amenable tumor types. To this end, the effect of various mutants on a variety of tumor cell lines that are derived from patients with brain tumors will be tested in an in vitro assay and an in vivo nude mouse system. The final phase of the application involves expanding Herpes therapy to an immunocompetent mouse model of primitive neuroectodermal tumors. This will elucidate the role of the immune system in modulating the efficacy of viral therapy since the majority of the human population is HSV-seropositive.

1F31MH012315-01
KIM, NORMAN
FUNCTIONAL MRI OF EMOTIONAL UNDERSTANDING IN AUTISM

UNIVERSITY OF CALIFORNIA
LOS ANGELES, CALIFORNIA

DESCRIPTION (Adapted from Applicant's Abstract): The proposed research is designed to extend our understanding of the neuropathology underlying one of the core behavioral characteristics of autism, deficits in emotional understanding. Autism is a severe and pervasive developmental disorder characterized by marked impairments in social relatedness and understanding, a integral component of which is emotional understanding and responsiveness. Previous empirical research on neurobiological substrate of these deficits has been limited by available methodologies. Recent advance in functional imaging technology allow for a more direct examination of the neural systems implicate in processing emotion, systems which are presumably damaged in individuals wit autism. FMRI will be used to measure in vivo, neural activity while participants watch film clips judged to depict examples of positive and negative emotions. These measurements will be obtained from 30 adolescents and adults with high-functioning autism and 30 matched non-autistic controls. It i hypothesized that (1) in the non-autistic sample, emotional stimuli will elici distinct patterns of neural activation, involving the limbic association cortex, and (2) positive, approach-related emotions will elicit activation distinct from negative, withdrawal-related emotions, involving hemispheric asymmetries. It is further hypothesized that (3) autistic participants will exhibit a pattern of neural activation distinct from non-autistic when presented with emotional stimuli, and (4) that autistic subjects will have difficulty with more complex, cognitively mediated emotions, such as embarrassment, that non-autistic subjects. This research is designed to add to our understanding of the underlying pathophysiology of autism, and to provide possible extension to neurological models of the understanding and processing of emotion in normal development.

1F32MH012274-01
KIRBY, LYNN
CRF EFFECTS IN THE DORSAL RAPHE NUCLEUS
ALLEGHENY UNIVERSITY OF HEALTH SCIENCES
PHILADELPHIA, PENNSYLVIA

DESCRIPTION (Adapted from Applicant's Abstract): Long-term exposure to stress has been implicated in the etiology of a number of psychiatric disorders such as depression. Both corticotropin-releasing factor (CRF) and the dorsal raphe nucleus (DRN)-5-hydroxytryptamine (5-HT) systems respond to stressors and have been independently implicated in depression. Anatomical studies have demonstrated that the DRN contains a dense population of CRF receptors and is richly innervated with CRF-immunoreactive fibers. AIMS 1 and 2 will test the hypothesis that CRF modifies the DRN-5-HT system by characterizing the effects of CRF on the activity of DRN 5-HT neurons in vivo and in vitro using extra-cellular and intracellular recording techniques, respectively. AIM 2 will also examine possible cellular mechanisms underlying CRF-HT interactions in the DRN. AIM 3 will test the hypothesis that these CRF-5-HT interactions are regulated by swim stress in an an animal model of depression and are potential targets of antidepressant treatment. These experiments will identify the role of CRF as a potential link between the stress response and the serotonergic dys-functions which characterize depression.

5F32MH011691-02
KIRKPATRICK-STEGER, KIM
SCHEDULE INDUCED BEHAVIOR IN RATS
BROWN UNIVERSITY

PROVIDENCE, RHODE ISLAND

DESCRIPTION (Adapted from Applicant's Abstract):
Although it is well-established that schedule-induced drinking occurs on intermittent schedules of food reinforcement, the mechanism by which drinking arises is still a mystery. The proposed experiments will test four major hypotheses. First drinking is a conditioned response that is controlled by the same basic laws as other conditioned responses. Second, drinking arises in anticipation of upcoming food delivery rather than occurring as a reaction to the previous pellet. Third, competition occurs between drinking and the operant, which can result in the displacement of drinking to the early portion of the interpellent interval. Finally, drinking may be controlled by timing mechanisms in much the same way as operant responses. The experimental results will be interpreted with three major theories of timing to determine whether the temporal locus and duration of bouts of drinking may be theoretically modeled in the same manner as operant responses such as lever pressing. If necessary, modifications in the theories will be made to accommodate the results of the proposed experiments.

1F30MH012083-01
KLEIN, AVNIEL
SEROTONERGIC MODULATION OF SENSORIMOTOR TRANSMISSION
MOUNT SINAI SCHOOL OF MEDICINE OF CUNY
NEW YORK, NEW YORK

Description (Adapted from applicant's abstract): Although many cellular actions of 5-HT have been described, consequences of these actions for behavior have been difficult to assess. Additionally, many studies have characterized relatively long lasting effects of serotonin that are important for processes related to learning and memory. In contrast, this study focuses on the B21/B8 synapse, a sensory-motor connection that is gated in that afferent activity is transmitted in a phasic manner that is controlled by an ongoing CPG. Experiments proposed will determine how this connection can be modulated by MCC activity without disrupting essential features of sensory-motor transmission. How MCC activity can up-modulate afferent activity in B21 and/or the transmission of this activity to B8 without disrupting the "gated" nature of the connection, and without increasing the excitability of B21 to the point where B21 no longer responds to changes in the characteristics of a peripheral stimulus, will be determined. Whether the MCCs accomplish this by exerting effects at a few key locations or whether effects of MCC activity are widespread will be determined. In summary, the MCCs, a pair of modulatory neurons whose contribution to behavior has been studied in intact animals, will be studied. How MCC activity alters transmission at a sensory-motor connection that is also experimentally advantageous in that it can be studied in semi-intact feeding preparations, as well as in reduced preparations, will be determined. In this study, therefore, insights will be gained both into mechanisms of action of serotonin, and physiological consequences of these actions for behavior.

1F32MH011714-01A1
KLOHNEN, EVA
WORKING MODELS OF ATTACHMENT--A SOCIAL COGNITIVE APPROAC
STANFORD UNIVERSITY
STANFORD, CALIFORNIA

DESCRIPTION (Applicant's abstract): Attachment research examines the role of internal working models--internalized representations of self and other that develop on the basis of early interactions--in directing cognitive, emotional, and behavioral response patterns. Social cognition research examines the role of cognitive structures in how people interpret, encode, and remember information they encounter in their everyday lives. Whereas the attachment-theoretical approach can inform about the development and role of social schemas in interpersonal behavior, the social cognitive approach can contribute an in-depth understanding of the ways in which these schemas influence social information processing and offer refined methodologies for studying them. The proposed program of research integrates the social cognitive and attachment- theoretical perspectives to advance understanding of the nature and content of working models, and to examine the processes through which they influence cognitive-affective response patterns. More specifically, this research has three aims: (1) to test whether internal working models of attachment constitute chronically accessible constructs (i.e., schemas) that affect the information processing of attachment-relevant stimuli; (2) to examine the effects of two kinds of priming--relational and non-relational--on information processing of individuals who differ in their attachment styles; and (3) to investigate specific cognitive mechanisms that might underlie the hypothesized biases in information processing that are characteristic of each attachment style.

1F31MH011983-01A1
KNAPP, LAUREN
REGULATION OF PKC BY REACTIVE OXYGEN SPECIES IN LTP
UNIVERSITY OF PITTSBURGH
PITTSBURGH, PENNSYLVANIA

DESCRIPTION: The objective of this research proposal is to better understand the biochemical mechanisms underlying long-term changes in neuronal function. The proposed studies will examine the biochemical underpinnings of hippocampal long-term potentiation (LTP), a widely studied cellular model for learning and memory. Specifically the investigation proposed will address the role of reactive oxygen species (ROS) as signaling molecules during LTP in area CAl of the rat hippocampal slices. The specific aims of this proposal are: 1) to test the hypothesis that ROS act as transient messengers to persistently activate protein kinase C (PKC) in hippocampal slices, 2) to test the hypothesis that ROS potentiate hippocampal synaptic transmission, and 3) to test the hypothesis that ROS potentiate hippocampal synaptic transmission via the activation of PKC. These specific aims will be addressed using direct enzymatic assays of PKC activity in hippocampal slices after incubations with various ROS-treatments. In addition, electrophysiological recordings will be performed on ROs/treated slices to assess the impact of ROS on synaptic transmission. The proposed work will provide important insights as to the functional significance of ROS as messengers that participate in processes mediating long-lasting synaptic plasticity.

1F31MH012147-01
KNOBELMAN, DEBORAH
SEROTONIN RELEASE AFTER DELETION OF AUTORECEPTORS
UNIVERSITY OF PENNSYLVANIA
PHILADELPHIA, PENNSYLVANIA

DESCRIPTION (Adapted from Applicant's Abstract):

Drugs that are effective in treating a number of psychiatric disorders appear to produce their effects by altering serotonin (5-HT) neurotransmission. The objective of this proposal is to examine the modulatory effects of the 5-HT 1A and 5-HT 1B receptors on the release of 5-HT in response to antidepressant drugs through the study of mutant mice with a constitutive deletion of either the 5-HT 1A or 5-HT 1B receptor. With either one of the presynaptic autoreceptors deleted, pharmacological challenges that increase the release of 5-HT (e.g., SSRIs) should demonstrate augmented effects on 5-HT release. Additionally, because both 5-HT 1A and 5-HT 1B receptors are involved in the presynaptic modulation of 5-HT release, they could potentially be part of compensatory mechanisms that develop when one of the receptors is deleted. These hypotheses will be assessed in several different studies. The effects of the novel 5-HT 1A receptor agonist 8-OH-PIPAT and the novel 5-HT 1B receptor agonist CP 94,253 on 5-HT release will be assessed in wild type mice. Both of these drugs shown distinct advantages over previously used drugs in pilot studies. Appropriate challenge conditions will be established. The effects of fluoxetine will then be assessed in 5-HT 1A and 5-HT 1B receptor knockout mice. These effects will subsequently be challenged by either a selective 5-HT 1A or 5-HT 1B receptor antagonist to assess the contributions to fluoxetine's effects of the 5-HT 1A receptor in 5-HT 1B receptor knockout mice and the 5-HT 1B receptor in 5-HT 1A receptor knockout mice. In mice with a constitutive deletion either of these autoreceptors, it is conceivable that the remaining autoreceptor may be involved in compensating for this specific loss of function. This hypothesis will be evaluated through pharmacological challenge of the 5-HT 1A receptor in the 5-HT 1B receptor knockout mice and the 5-HT 1B receptor in the 5-HT 1A receptor knockout mice under conditions developed above. In addition, pilot studies have shown a potentiated hypothermic response to 8-OH-DPAT, a 5-HT 1A receptor agonist, in 5-HT 1B receptor knockout animals. This effect will be assessed as a complementary physiological response that is sensitive to activation of distinct receptor subtypes. Finally, quantitative receptor auto-radiography will evaluate the quantity of 5-HT 1A and 5-HT 1B receptors in these mice. A greater understanding of the modulatory effects of the 5-HT 1A and 5-HT 1B receptors on the release of serotonin through their genetic deletion could lead to a better understanding of genetic contributions to differing sensitivities of humans to antidepressant treatment.

1F31MH011954-01
KOENEN, KARESTAN
COMORBIDITY OF PTSD AND ANTISOCIAL PERSONALITY DISORDER
BOSTON UNIVERSITY
BOSTON, MASSACHUSETTS

DESCRIPTION (Adapted from applicant's abstract): High rates of comorbidity between PTSD and antisocial personality disorder (APD) have been documented in both veteran and civilian samples. This comorbidity is of great concern to both researchers and clinicians. For other mental disorders, comorbidity with APD has been associated with treatment complications, a more severe course of illness, and greater impairment for the suffering individual in a wide variety of areas. To date, the nature of the relationship between these disorders remains unclear.
This study seeks to conduct secondary data analysis using the resource presented by the Vietnam Era Twin Registry (VETR) to clarify the factors

that influence the established high rates of comorbidity found between Antisocial Personality Disorder (APD) and Posttraumatic Stress Disorder (PTSD) in Vietnam veterans. Previously, the VA-supported Survey of Health (1987) and the NIDA-supported Harvard Twin Study of Drug Abuse and Dependence collected demographic, military service, combat exposure, and diagnostic data on 3,234 male-male pairs of monozygotic (MZ) and dizygotic (DZ) twin pairs who range in age from 38-56 (mean age=45). All pairs are comprised of twins who both served on active military duty during the Vietnam era. These data will be used for two main purposes. First, twin methodology will be used to determine the role familial and genetic influences play in the comorbidity of these two disorders. Second, co-twin control methodology will be used to address the variety of methodological limitations which have plagued research in this area.

5F32MH011461-02
KOGAN, JEFFREY
LONG-TERM POTENTIATION AND MEMORY IN CREB MUTANT MICE
COLD SPRING HARBOR LABORATORY
COLD SPRING HARBOR, MAINE

DESCRIPTION (Adapted from Applicant's Abstract):
Recent results from the Silva laboratory show that mice with a targeted disruption of the cAMP. -responsive-element binding protein (CREB) gene (CREB-/-) have normal short-term, but deficient long-term responsive-element binding protein (CREB) gene (CREB-/-) have normal short-term, but deficient long-term memory. This behavioral phenotype is paralleled by deficits in hippocampal CA1 long-term potentiation (LTP). The principal objective of this proposal is to determine how CREB modulates short and long-term changes in the physiology of hippocampal CA1 neurons and how these changes may affect behavior. Extracellular and whole-cell recording methods will be used to examine LTP and long-term depression in hippocampal brain slices prepared from CREB mutant mice. I will test the hypothesis that different protocols for LTP induction and fear conditioning can alleviate the deficits of the mutants. Pharmacological treatments which a) modulate the cAMP pathway and b) inhibit protein synthesis, will allow me to determine if the CREB mutation has an impact on biochemical pathways which may be modulating neuronal plasticity. The use of whole-cell recording methods will allow a detailed examination of the electrophysiology of the mutant cells including a comparison of the intrinsic membrane properties and the characteristics of action potentials in WT and mutant neurons. Whole-cell recordings will also be used to determine whether synaptic currents are altered in CREB mutant neurons. Findings in Aplysia, Drosophila and mice indicate that the cellular mechanisms involving CREB in memory are evolutionarily conserved. Thus, the experiments proposed here will have an impact on tahe understanding of cellular mechanisms supporting human memory.

5F31MH011716-02
KOZIOL-MCLAIN, JANE
SCREENING FOR PARTNER VIOLENCE--A NURSING INQUIRY
UNIVERSITY OF COLORADO HLTH SCIENCES CTR
DENVER, COLORADO

DESCRIPTION (Adapted from Applicant's Abstract):
Violence among intimate partners is a significant heaalth problem for women in the Unites States. Nursing organizations and public health officals now mandate that all clients be screenes for violence and that

policies be in place for idenifiying and treating vivtims of partner violence. However, these mandates for partner violence screening are untested. The purpose of this prospective cohort study is to test whether a postive screen for past partnet violence is a maker for future violent espisodes. Specific aims for this population-based study are to: (1) Describe the rates of partner violence based on a telephone administer screen assessing one-year period prevalence of physical abuse; (2) Secribe the three-months rate, pattern and severity of partner violence against women based on an in-depth structured telephone interview; (3)Determine the likelihood of short-term abuse based on a positive partner violence screen; (4) Describe the rates of community service use by abused women; and, (5) Determine whether ethnicity, geopgraphy region)that is, rual versus urban), or income level influence the ability of a partner violence screen to prefict future partner violence. Women will be interviewed three months after they have completed an Injury Control Module partner screen. The frequency, severity, and pattern of abusive events in the three months following the screen will be measured in structured telephone interview that includes the Confict Tactics Scale (CTS, Straus. 1992). Violent episodes will be compared across ethnic, geographic, and income level groups. Research methods are developed from femnist perspective with women;s safety as a priority. Interviews with women will be based on a model of empowerment (campbell and Parker, 1996; Campbell, Smith mc Kenna, Torres, Sheridan, and Landenburger, 1993). The Knowledge gained in this study will provide important information about the pattern of violence in a population-based smaple of women liviing in the community. This study will provide the naseline rate and description of violent espisodes for planning subsequent nursing research testing the effects of a nursing partner violence intervention.

5F31MH011270-02
KOZLOSKI, JAMES
NEURAL PROCESSING OF COMMUNICATION SOUNDS
UNIVERSITY OF PENNSYLVANIA
PHILADELPHIA, PENNSYLVANIA

DESCRIPTION (Adapted from Applicant's Abstract):
The research proposed here is directed toward developing a better understanding of how critical features of communication signals are coded and processed by neural circuits in the brain. The specific goal is to elucidate neurobiological processes which are fundamental to natural auditory communication. Auditory nervous systems have the task of processing important timing cues in communication signals, whether in human speech or in the acoustic communication of a diverse array of other vertebrate animals. The basic organization of auditory pathways is similar across vertebrate classes, and certain species of vertebrate animals are particularly valuable for addressing issues relating to the neurobiology of hearing, communication, and the learning processes which they subsume.
In particular, the neurophysiological studies proposed here address problems in fundamental neuroscience which are potentially relevant to import mental health issues, including the design of treatments for individuals with auditory-related learning dysfunctions. Recent studies suggest that poor discrimination of auditory time cues by language impaired children may lie at the root of a broad spectrum of learning disorders.

The proposed research focuses on the neural processing of time features in the auditory system of a vertebrate animal which uses a limited set of simple sounds for courtship communication. By conducting neuroanatomical and neurophysiological experiments in the auditory brainstem of Pollimyrus (ie., auditory nerve to midbrain), the substrate and method for the coding of temporal features in sonic stimuli will be examined. New knowledge about how the normal vertebrate nervous system responds to these signals will contribute to the basic biomedical science needed to design informed treatments of dysfunction.
The fish (Pollimyrus) is an excellent animal model for this research because: 1. Its repertoire of sounds has been carefully characterized, 2. The dominant features of its sounds are temporal patterns, and 3. Its ear appears to be adapted time analysis (the animal~s hearing is based on an array of hair cells like that found in the human ear, but it does not posses a mechanical frequency analyzer like in the mammalian cochlea).
This animal has also proven to be outstanding for single neuron physiological studies and for anatomical studies of the auditory pathway. The proposed research combines neurophysiological studies of the auditory system with neuroanatomical pathway tracing from those auditory centers which have been characterized physiologically. Having made a careful choice of an appropriate animal model, I expect that progress will be made toward a better understanding of fundamental mechanisms of vertebrate communication.

5F30MH011504-03
KRASOWSKI , MATTHEW
MOLECULAR MECHANISMS OF BARBITURATES AT GABA-A RECEPTORS
UNIVERSITY OF CHICAGO
CHICAGO, ILLINOIS

DESCRIPTION (Adapted from applicant's abstract): Many structurally different classes of compounds with central nervous system (CNS) depressant effects, such as the barbiturates, general anesthetics, neurosteroids, alcohol, and the benzodiazepines, modulate synaptic inhibition mediated by the GABAA receptor (GABAA-R) in the mammalian CNS. In many cases this is likely to be the primary mechanism by which these drugs induce acute intoxication, provide clinically useful therapy, exert side effects, and/or mediate abuse liability. The molecular nature of the interaction of these agents with the GABAA-R is not well understood and, with the exception of the benzodiazepines, the sites of binding have not been characterized. The goals of the proposed research are to study the pharmacology and electrophysiology of chimeric receptors containing portions of human GABAA-R subunits together with complementary pieces of the related glycine receptors or the GABAA pi subunits (the 'GABAc receptor'). In particular, the proposed research will focus on the barbiturates. These chimeras were chosen to combine homologous ligand-gated receptor subunits that are modulated by barbiturates (e.g., GABAA-Rs) with those that are insensitive to barbiturate modulation (e.g., the pi subunit to gain information about the molecular nature of the sites of interaction.

5F32MH011808-02
KRUPA, DAVID
NETWORK LEVEL PROPERTIES OF SOMATOSENSORY PLASTICITY
DUKE UNIVERSITY
DURHAM, NORTH CAROLINA

DESCRIPTION (Adapted from applicant's abstract): The long-term goal of this application is to elucidate the neural circuit level properties and mechanisms which underlie the immediate and pronounced reorganization of sensory maps in the somatosensory system caused by local anesthesia of the face. The basic hypothesis is that sensory representations in the somatosensory system are not "hard wired", but, instead, represent a "dynamic equilibrium" between both feed forward and feedback influences on sensory processing neurons. This hypothesis predicts that inactivation of any particular part of this system should cause rapid and compensatory changes throughout much of the rest of the system. The specific aims of this proposal are to characterize the role of the somatosensory cortex (SI), the posterior medial nucleus of the thalamus (POm), and the spinal trigeminal (interpolaris) nucleus (SpV) in the reorganization of somatotopic maps caused by peripheral anesthesia. These goals will be accomplished by recording single unit activity of many neurons simultaneously through arrays of microwire electrodes implanted at multiple levels of the trigeminal sensory pathway of rats while either SI, POm, or SpV is reversibly inactivated by focal micro-injections of the GABA-A agonist muscimol. Quantitative measurement of the receptive fields of each neuron as well as "population maps" will be determined prior to focal inactivations. These same measures will be repeated during the inactivations and again following recovery. These measurements will allow precise quantitative determination of the time course of induced changes in sensory representations resulting from these inactivations. These results will provide further insight into the understanding of now only how the brain processes information normally but how the brain recovers from injury, an understanding which is crucial for developing improved means of treating such injuries.

5F32MH011723-02
KURTZ, KENNETH
FOUNDATIONS OF SIMILARITY AND CONCEPTUAL STRUCTURE
NORTHWESTERN UNIVERSITY
EVANSTON, ILLINOIS

DESCRIPTION (Applicant's Abstract): Categorization and inductive forms of reasoning are traditionally thought to be grounded in similarity, but recent arguments have challenged the explanatory power of similarity (Murphy & Medin, 1985). The goal of the present proposal is to investigate a mechanism of functional re-representation as a basis for the construction of concepts held together by an enriched form of similarity. This mechanism is instantiated in connectionist terms based on the back-algorithm (Rumelhart et al., 1986). Learning involves adjusting parameters to achieve a functional similarity whereby like internal representations lead to like outputs (Rumelhart et al., 1995). Like kinds emerge as an integration of 1) structural constraints derived from the correlational structure present in the environment, and 2)functional constraints induced by task-mappings from perceptual inputs to useful abstract commonalities. The psychological validity of this approach will be tested in a series of experiments. Additionally, an attempt will be made to find common ground between functional re-representation and the view of similarity comparisons as a process of structural alignment (Gentner &Markham, 1995).

1F30MH012163-01
LADD, CHARLOTTE
CORTICOTROPIN RELEASING FACTOR IN A RAT DEPRESSION MODEL
EMORY UNIVERSITY
ATLANTA, GEORGIA

Early maternal separation is a model of major depressive disorder, as numerous preclinical studies have demonstrated that maternally-separated (MS) animals exhibit behavioral, physiologic, and neuroendocrine aberrations characteristic of depression. For example, both untreated depressed patients and MS rats experience an apparent increase in limbic and hypothalamic expression of corticotropin-releasing factor (CRF), a neuropeptide which coordinates the mammalian stress response. Utilizing this maternal separation model, we aim to test the hypotheses that CRF is involved in the pathophysiology of depression and serves as a common mediator of antidepressant efficacy. These hypotheses will be investigated in six specific aims. The first and second experiments will evaluate basal and stress-induced regional CRF and CRF receptor expression in MS rats vs. controls. The third and fourth experiments will establish whether or not chronic treatment with three pharmacologically-distinct antidepressants reverses the maternal separation phenotype and selectively decreases regional CRF expression in MS rats, thus supporting or refuting the hypothesis that CRF is a common mediator of antidepressant efficacy. The fifth and sixth experiments will test the hypotheses that, following antidepressant withdrawal, chronically-treated maternally-separated rats relapse into the maternal separation phenotype and exhibit a temporal increase in regional CRF expression. These experiments will provide further evidence to support or refute CRF's role in the pathophysiology of depression and determine whether or not this peptide is a common mediator of antidepressant efficacy.

1F31MH012189-01
LARSEN, JEFF
HENDONICS IN THE BRAIN--A ERP ANALYSIS
OHIO STATE UNIVERSITY
COLUMBUS, OHIO

DESCRIPTION (Applicant's abstract): Whereas affect has traditionally been conceptualized on a bipolar continuum ranging from positive to negative, Cacioppo and Berntson's (1994) bivariate model of evaluative space posits separable dimensions of positivity and negativity. The nature of evaluative processes bears upon our understanding of affective disorders, particularly in light of the notion that a general down- regulation of affect underlies depression. In bivariate terms such down-regulation may in fact be mediated by specific dysfunction of positive and/or negative activation. Our aim is to test whether the late positive potential (LPP) of the ERP can index the separability of positivity and negativity. Participants will make evaluative categorizations of very positive, mildly positive, and mildly negative trait words embedded in a mildly positive context. Insofar as the LPP indexes the separability of positivity and negativity, mildly negative (opposite-valence) targets will produce larger LPPs than very positive (same-valence) targets. Other participants will make evaluative categorizations of mildly positive, mildly negative, and very negative trait words embedded in a mildly negative context. Here mildly positive (opposite-valence) targets are expected to evoke larger LPPs than very negative (same-valence) targets. In both conditions, bipolar models predict that same-valence and opposite-valence targets will evoke comparably large LPPs.

1F31MH012085-01
LARSON CHRISTINE

REGIONAL BRAIN FUNCTION AND EMOTIONAL REACTIVITY
UNIVERSITY OF WISCONSIN
MADISON, WISCONSIN

DESCRIPTION (Applicant's abstract): This project proposes the use of multiple physiological methods to: 1) develop an objective measure of trait-like patterns of affective responding, and 2) to better understand the relations between individual differences in the time course of emotional reactions, and the neural substrates underlying emotional experience. Despite the growing body of emotion research, few objective, non-self-report induces of emotional experience exist, and very little work has been done examining the temporal course of responses to an emotion elicitor. The time course of emotions may be a very important variable in understanding individual differences in affective style. For example, individuals who experience negative emotions longer may be more likely to become anxious or depressed. To address the first goal, developing an objective measure of trait affective responding, the stability of the emotion-modulated startle response will be assessed to determine whether this paradigm shows suitable reliability for use as a trait -like index. The second goal, understanding the chronometry of emotions, will use subjects with extreme asymmetry of frontal EEG activation (shown previously to be related to state and trait affect) to examine individual differences in the time course of cortical and subcortical brain activation (measured with FMRl) in response to affectively-laden pictures.

5F31MH011745-02
LAWRENCE, ERIKA
VIOLENCE & THE LONGITUDINAL COURSE OF NEWLYWED MARRIAGES
UNIVERSITY OF CALIFORNIA
LOS ANGELES, CALIFORNIA

DESCRIPTION (Adapted from applicant's abstract): The proposed research is designed to add to existing knowledge on violence and the longitudinal course of newlywed marriage. Newlywed couples (N=172) were assessed six months postmarriage for violence and variables found to covary with marital violence, both intrapersonally (i.e., alcohol and drug abuse, stressful life events, depression, psychiatric disorders) and interpersonally (i.e., psychological abuse, negative and positive affect and withdrawal during conflict, and marital distress). Violence is hypothesized to covary with significantly more of these variables than nonviolence. Further, severe or unidirectional violence is hypothesized to covary with more of these variables than mild orbi directional violence. Such findings would suggest that prevention programs target the cessation of violence and these covariates. Marital quality and stability will be examined eight times, every six months over four years to examine their developmental course. Violent couples are hypothesized to experience greater marital decline than nonviolent couples. Further, the covariates described are expected to moderate the association between violence and marital decline, such that when violence covaries with several of these variables, compared to few or no covariation, marital decline is expected to be greater. Such findings would suggest targeting those factors that affect marital outcomes. Finally, violence will be assessed eight times; it is hypothesized that stably aggressive couples will experience the greatest marital decline, followed by instably aggressive and stably nonaggressive couples, respectively. In sum, the proposed research is designed to enhance basic research relevant to the prevention of intimate violence and marital deterioration.

5F31MH011531-02
LE BELLE, JANEL
APPLICATIONS OF 1H NMR SPECTROSCOPY TO NERVOUS SYSTEM
UNIVERSITY OF LONDON INST OF CHILD HLTH
LONDON, UNITED KINGDON

DESCRIPTION (Adapted from applicant's abstract): Previous studies (Urenjak, et al., 1993; Florian, 1995) have shown that the metabolic profiles revealed by proton NMR spectroscopy can be useful to distinguish unambiguously between different brain cell populations. In addition, 1H-NMR spectra could similarly be used to distinguish between different types of tumors of the human nervous system and to relate tumor populations to their cell type of origin. Preliminary data suggest that these spectra may enable the identification of metabolic changes associated with conditional on cogene activation, and that certain metabolite differences may allow normal brain cells to be distinguished from their transformed counterparts. This would allow for the noninvasive, nonsurgical diagnosis of human central nervous system (CNS)tumors. The research for the applicant's dissertation will use 1H-NMRspectroscopy in vitro, in order to compare normal and tumor cells of the same lineage in order to test the hypothesis that 1H-NMR spectroscopy can be used both to determine the lineage of a tumor cell and to investigate metabolic alterations that may distinguish tumor cells from normal cells. In addition, the applicant's research will include 1H-NMR spectroscopy of superfused cell sex vivo, in order to relate spectra from the in vitro cell extracts to the in vivo situation of observing metabolizing cells. Finally, the applicant's research will include 1H-NMR spectroscopy of implanted tumor cells in the rat brain in vivo, in order to obtain information that would aid the noninvasive diagnosis by NMR spectroscopy of various types of human brain tumors, in terms of their histological origin and degree of malignancy. The ultimate goal of this research is the identification and regulation of the pathways which maybe differentially activated in tumor cells, and of the specific metabolic changes characteristic of the transformation process of various cell types of the CNS.

1F31MH011995-01A1
LEE, HOSUK
MOLECULAR GENETICS STUDY OF SYNAPTIC TRANSMISSION
PURDUE UNIVERSITY
WEST LAFAYETTE, INDIANA

DESCRIPTION (Adapted from applicant's abstract): The long-term goal of this research is to contribute to the understanding of the mechanism of synaptic transmission. The specific aim of the proposed project is to identify a novel protein involved in synaptic transmission by the "forward genetic" methods using Drosophila and to characterize the in vivo function of the molecule using various genetic, molecular biological, and electrophysiological methods. Three Drosophila mutants belonging to a single complementation group display abnormal histamine distribution in photoreceptors and blocked histamine release, suggesting that they are defective in presynaptic mechanisms of the photoreceptor synaptic process. A 3kb cDNA that most likely corresponds to the gene identified by these mutants has been isolated and completely sequenced. It contains an open reading frame which encodes a novel protein of 953 amino acids but is still open at the 5' end. Immediate goals of the project include isolation of cDNA clones with complete open reading frames, demonstration that the cDNA identified does in fact correspond to the gene, and functional analysis of the protein encoded by the cDNA. Since synaptic transmission is a

fundamental property of the nervous system and its overall mechanism is conserved among organisms ranging from yeast to humans, the identification of a molecule important for synaptic transmission in Drosophila is likely to contribute to the understanding of the mechanisms of synaptic transmission in general, including that in humans.

1F30MH012173-01
LIN, SHAO-POW
MR STUDY OF BRAIN INTERSTITIAL WATER MOTION
WASHINGTON UNIVERSITY
St. Louis, Missouri

DESCRIPTION (Adapted from applicant's abstract): Brain water motion, which can be detected by MR techniques, varies depending on many factors, some characteristic of normal physiology and others of pathology. As a result, diffusion weighted imaging is used widely for the evaluation of a number of CNS states. Maintenance of water motion is either itself important for normal brain function or is at least an excellent marker of physiologic state. The Neil/Ackerman laboratory's research program focuses on elucidating the factors which determine water motion. This proposal focuses on learning more about the contribution of extracellular water to the total (intra- plus extracellular) water ADC. Motion in the interstitial fluid has contributions from bulk cerebrospinal fluid (CSF) flow, compartmental boundaries, and Brownian motion. Experiments were designed to determine the relative contribution of these three factors to ADC. The interstitial water ADC will be measured indirectly by measuring the motion of a broad range of extracellular markers. Recent results show that ADCs of compounds confined to the extracellular space are approximately equal despite marked differences in molecular weight (MW). This suggests that bulk CSF flow is a dominating factor. This idea will be tested with both large extracellular markers (polyethyleneglycols of MW=0.9 and 4 kD) and one very small marker (sodium, MW=23). Finally, CSF flow will be pharmacologically altered to directly assess its effect on extracellular water ADC.

1F31MH012193-01
LINSEMAN, DANIEL
MUSCARINIC RECEPTOR SIGNALING TO FOCAL ADHESION KINASE
UNIVERSITY OF MICHIGAN
ANN ARBOR, MICHIGAN

DESCRIPTION (Adapted from applicant's abstract): Synaptic plasticity plays a significant role in learning, memory, and CNS development. The tyrosine kinase focal adhesion kinase (FAK) acts as a regulator of neurite outgrowth mediated by phosphoinositide-linked receptors. Elucidation of the mechanism by which these receptors signal to FAK may aid in understanding the pathways underlying synaptic plasticity. The proposed research focuses on the role of inositol lipids in regulating m3 muscarinic receptor (mAChR) signaling to FAK. Specific Aim 1: To determine if mAChR signaling to FAK is attenuated by blockade of inositol lipid synthesis via overexpression of a dominant-negative mutant or phosphatidylinositol 4-kinase (P14K). The effects of a dominant-negative mutant of PI4Kbeta on mAChR signaling to FAK will be assessed in stably transfected SH-SY5Y neuroblastoma cells by analysis of FAK phosphorylation and in vitro kinase assays of FAK catalytic activity. Specific Aim 2: To evaluate if inositol lipids indirectly regulate mAChR signaling to FAK via effects on the actin cytoskeleton. The effects of phosphoinositide depletion on agonist-induced cytoskeletal remodeling and actin uncapping will be assessed by immunocytochemical

analysis of F-actin redistribution and co-immununoprecipitation assays of actin/gelsolin complexes, respectively.

1F31MH011872-01A1
LIVINGSTON, FREDERICK
ACTIVITY AND LMAN DURING SONG DEVELOPMENT
DUKE UNIVERSITY
DURHAM, NORTH CAROLINA

DESCRIPTION (adapted from applicant's abstract): The central goal of this proposal is to understand the role of activity in LMAN during song development. First, activity will be removed from LMAN by using reversible pharmacological lesion, and it is hypothesized that this will cause an increase in song stereotypy similar to permanent lesions of LMAN. To determine whether LMAN can have acute effects on song, activity will be induced in LMAN using direct electrical stimulation. This experiment will address the question whether LMAN can produce vocalizations or disrupt ongoing song during sensory motor learning. Also, LMAN will be chronically stimulated throughout sensory motor learning to observe how LMAN can affect song quality long-term.
The second part of this proposal will determine the relevance of low-threshold Ca++ spike, (LTS) present in only young zebra finch LMAN neurons, to sensory acquisition. This first will be tested by recording intra-cellularly from LMAN neurons from acoustically isolated zebra finches. Isolating zebra finches serves to extend the critical period of sensory acquisition, and thus should also delay the disappearance on the LTS. Next, an antagonist of the LTS will be infused into LMAN via cannulae to determine whether blocking the LTS can decrease the amount of syllables a young zebra finch can copy from its tutor during song learning.

1F31MH012108-01
LLOYD, THOMAS
HRS AND SYNAPTIC TRANSMISSION
BAYLOR COLLEGE OF MEDICINE
HOUSTON, TEXAS

DESCRIPTION (Adapted from applicant's abstract): The goal of this research proposal is to develop a better understanding of the mechanisms underlying synaptic transmission through the characterization and mutational analysis of Hrs, a protein recently implicated in neurotransmitter release. Docking and fusion of synaptic vesicles with the presynaptic membrane is thought to require a core complex formed by three proteins: synaptobrevin, SNAP-25, and syntaxin. In an attempt to identify proteins that interact with this core complex in mouse, Bean et al. (1997) performed a yeast two hybrid screen with SNAP-25 as bait. This led to the identification of Hrs, a cytoplasmic protein that is highly expressed in the brain, specifically binds SNAP-25, and contains an FYVE zinc finger domain commonly found in proteins involved in vesicle transport in yeast and vertebrates. Furthermore, addition of recombinant Hrs to permeabilized PCl2 cells inhibited neurotransmitter release, suggesting that Hrs plays a role in this process. We have recently cloned and sequenced the Drosophila homolog of hrs, and have mapped the gene to a well-characterized region in the Drosophila genome. Here, we propose to examine the in vivo role of Hrs in neurotransmitter release in Drosophila. First, we will determine the tissue and subcellular localization of Hrs and perform a biochemical analysis of the interactions of Hrs with other proteins involved in synaptic transmission. We will then isolate mutations in Hrs and characterize them

molecularly and genetically. Finally, and most importantly, electrophysiological studies will be carried out to determine the effects of these mutations on neurotransmitter release in vivo. The dissection of the function of Hrs through electrophysiological and biochemical analysis should yield important insights into the mechanisms of synaptic vesicle release. An understanding of this mechanism may contribute to medically relevant issues such as drug action at the synapse, disease states associated with changes in neurotransmitter release, and the processes underlying learning and memory.

5F31MH011518-03
LOFTUS, WILLIAM
FUNCTIONAL ORGANIZATION OF AUDITORY CORTEX
UNIVERSITY OF CALIFORNIA
DAVIS, CALIFORNIA

DESCRIPTION (Adapted from Applicant's Abstract):
The long-term goal of the proposed research is to understand how the functional divisions of auditory cortex relate to the analysis of complex sounds. Investigation will focus on the processing of intensity and temporal information in the auditory central nervous system (CNS) of the cat. The anatomical connections and architectonic parcellation of this system is well studied but much less is known about its functional organization. Two cortical regions: primary auditory cortex (AI) and posterior auditory field (PAF) will be the subject of physiological studies with these specific aims: l) to investigate the relationship between the response properties of geniculocortical afferents and the cortical cells to which the afferents provide input, and 2) to investigate the subconical organization of those afferents. Electrophysiological recordings will be acquired in either hemisphere of anesthetized cats under contralateral ear stimulation. For aim 1, single cortical neurons will be characterized in terms of their intensity tuning or temporal integration properties. The response of the cortical cells will then be pharmacologically silenced, which will enable recording from thalamic afferents in the same electrode penetration. For aim 2, recordings will be made from the cell bodies of afferents while simultaneously recording from cortical cells to which they provide input. The afferent recordings will be compared to the cortical recordings and interpreted in terms of the cortical transformations of afferent inputs. The subcortical organization of the inputs to PAF and AI will be compared and interpreted in terms of parallel and hierarchical organization of function. The results of these investigations will be relevant to understanding the basis of auditory perception and disturbances in auditory perception due to acquired lesions, developmental learning impairments, and schizophrenia.

1F32MH011695-01A1
MACDOUGAL-SHACKLETON, SCOTT
EARLY LEARNING EFFECTS ON ADULT NEUROENDOCRINE SYSTEM
PRINCETON UNIVERSITY
PRINCETON, NEW JERSEY

DESCRIPTION (adapted from applicant's abstract): This study will examine the effects of early learning on the adult neuroendocrine system. Specifically, it will examine the physiological and behavioral response of female white-crowned sparrows (Zonotrichia leucophrys oriantha) to male songs with which they have, or have not, had prior experience. White-crowned sparrows learn their songs during a sensitive phase early in

life, but respond to these songs in adulthood. Juvenile females sparrows will be captured from their natal area and housed in captivity. Then they will be stimulated by long days and played back male courtship songs from either their natal area or another area. Songs from another species and no song will be used as control treatments. Behavioral responses to be examined will be nest-building and solicitation displays. Physiological responses to be examined will include ovarian development and circulating hormone levels. Photoperiodic species of birds exhibit remarkable plasticity in the size and number of neurons immunoreactive for gonadotropin releasing hormone (GnRH), and changes in this system will also be measured. Hormone levels will be determined by radioimmunoassay. Immunoreactive GnRH neurons will be measured by immunocytochemistry. These experiments will test two hypotheses: i) that young female white-crowned sparrows imprint on the song of their natal area, and that in adulthood this learned song facilities both reproductive behavior and neuroendocrine responses to photo-period; ii) that this physiological response to song is mediated directly by the hypothalamo-pituitary-gonad axis.

1F31MH012199-01
MACEK, THOMAS
MODULATION OF MGLUR7 FUNCTION BY PROTEIN KINASE C
EMORY UNIVERSITY
ATLANTA, GEORGIA

DESCRIPTION (Adapted from applicant's abstract): The hippocampus plays an integral role in a number of normal physiological processes and in various pathological conditions. Fast synaptic transmission is modulated by activation of a family of G protein-coupled glutamate receptors, termed metabotropic glutamate receptors (mGluRs), which can serve as autoreceptors at glutamatergic synapses. Evidence suggests that one mGluR subtype, mGluR7, serves as an autoreceptor at the Schaffer collateral-CA1 synapse. Our preliminary data demonstrate that mGluR7-mediated autoreceptor function at this synapse can be inhibited by activation of protein kinase C (PKC) by phorbol esters or A3 adenosine receptor activation. At present, the mechanism by which PKC inhibits mGluR7 autoreceptor function is not known, yet PKC inhibits signalling of group I mGluRs by a direct phosphorylation of the receptor protein. We postulate that PKC inhibits mGluR7-mediated responses by direct phosphorylation of mGluR7. The proposed studies will elucidate the mechanism by which PKC modulates signalling of mGluR7. A series of biochemical and molecular biological studies is proposed to directly test this hypothesis.

1F31MH011956-01A1
MAE, LYNDA
SPONTANEOUS TRAIT TRANSFERENCE IN PREJUDICED SPEECH
PURDUE UNIVERSITY
WEST LAFAYETTE, INDIANA

DESCRIPTION (Adapted from applicant's abstract): The proposed research investigates the consequences of prejudiced speech. Based on recent research on spontaneous trait transference, I propose that those who express bigotry actually become associated with the very traits they describe in out-groups. I advance the counter-intuitive prediction that these trait associations occur even for in-group perceivers who are similarly prejudiced themselves. Furthermore, this research will demonstrate that these trait associations have a number of social consequences for prejudiced speakers. In particular, as a result of bigoted remarks, perceivers will actually

attribute the implied traits to the prejudiced communicators, will bias their interpretations of subsequent communicator behaviors, and will be reluctant to engage in certain interactions with communicators. This research will advance our understanding of three areas of social psychology: spontaneous trait transference, social effects of simple associations, and reactions to prejudice. It will also extend the methodologies used in impressional research by employing relatively naturalistic stimuli and relatively novel measures of social perception. Finally, my findings may suggest strategies for discouraging overt expressions of bigotry.

5F32MH011573-02
MAFFI, LUISA
FOLK ECOLOGICAL COGNITION
NORTHWESTERN UNIVERSITY
EVANSTON, ILLINOIS

DESCRIPTION (Applicant's Abstract): This proposal focuses on training and research on the structure and content, as well as processes, of humans' ecological knowledge, and on the relationships between this knowledge and natural resource management practices. The successful solution of environmental problems requires the identification of the psychological as well as sociocultural factors that operate within given populations, interacting with the features of local ecosystems in ensuring sustainable resource management. Under increasing global pressure over the world's ecosystems, the livelihood and nutritional and health status of millions of people on earth may depend on the preservation and promotion of local ecological knowledge and resource management solutions. The present research will create a bridge between the study of folk biology and that of common-pool resource management, by concentrating on several aspects of ecological knowledge and reasoning among study populations in Guatemala, Mexico, and the US: 1) identification of the role of ecological vs. morphological factors in category-based inductions on local species; 2) elicitation of classification of ecological features such as soils, waters, species subcommunities; and 3)elicitation of beliefs on the ecological significance and interdependencies of local species. The resulting mental models of the environment will then be tied to agroforestry practice in the effort to establish causal links between belief and behaviors.

5F32MH011850-02
MAHONEY, JOSEPH
DEVELOPMENT AND PREVENTION OF ANTISOCIAL PATTERNS
STOCKHOLM UNIVERSITY
STOCKHOLM, SWEDEN

DESCRIPTION (Adapted from applicant's abstract): The research to be undertaken as part of this postdoctoral fellowship involves a cross-national comparison of the development of antisocial and criminal behavior across four longitudinal data sets. Research samples include the Individual Development and Adaptation study and the Young Lawbreakers as Adults study at Stockholm University, Sweden, The Solna Project at Orebro University, Sweden, and the Carolina Longitudinal Study at the University of North Carolina at Chapel Hill in the United States. Each study has tracked the participants from childhood through adulthood, and each study maintains a rich data source on antisocial and criminal behavior. The major objectives of the proposed study are: (1) to describe the developmental antecedents of adult antisocial and criminal behavior during childhood and adolescence using a person-oriented approach to

analysis; (2) to clarify gender-related differences in antecedents and pathways toward antisocial and criminal outcomes; (3) to assess the role of participation in extracurricular activities as a possible moderator of antisocial patterns among high-risk youth; and (4) to determine the extent to which cross-national generalizations may be drawn on risk and resilience factors. First, developmental antecedents to subsequent deviance and criminality will be evaluated from a person-oriented, holistic perspective that focuses on the ways in which biological, psycho-social, and contextual factors work in tandem to support behavioral outcomes across development. Second, potential gender differences will be explored with particular interest in the role of maturational timing and non-physical aggression in the development of female antisocial patterns and criminality among high risk youth will be assessed. The turning points include patterns of educational attainment and engagement in extracurricular activities during adolescence. Finally, the availability of comparable data sets from research sites in different countries during the same temporal period will permit the detailed analysis of cross-national similarities and differences in factors of risk and resilience.

5F30MH011432-03
MAIER, JOHN
NONINVASIVE NEAR INFRARED NEONATAL BRAIN HEMOXIMETRY
UNIVERSITY OF ILLINOIS AT CHICAGO
CHICAGO, ILLINOIS

DESCRIPTION (Adapted from applicant's abstract): Near-infrared tissue spectroscopy in advancing toward clinical use in many areas of medicine. The study of the brain both in terms of hemoximetry and neurophysiological signals is the primary focus of much of the current research in this area. The applicant's laboratory has pioneered the development of a near-infrared tissue spectrometer for clinical use based on the physical understanding of how light travels in tissues. This physical model assumes a homogenous infinite tissue bounded by a flat plane. The applicant proposes to investigate two of the fundamental problems involved with application of this model to near-infrared spectroscopy of the brain: the problem of the curved surface of the skull, and the problem of light piping by the cerebrospinal fluid (CSF). Though these problems are present in both adults and infants, the applicant will focus on them in the neonatal case. Neonatal brain hemoximetry is of interest because of the correlation of long-term pathology including cerebral palsy, attention deficit disorder and mental retardation, with ischemic and hemodynamic insults to neonates. The applicant will investigate the accuracy of a simple model for curved surfaces through in vitro laboratory experiments on tissue simulating phantoms. He will also explore, through Monte Carlo modeling and experimental studies on in vitro laboratory samples, the degree to which the CSF is expected to affect the measurement protocols currently in place.

5F32MH011703-02
MARTIN, WILLIAM
EVOLUTION OF SOCIAL COMMUNICATION IN ANURAN AMPHIBIANS
UNIVERSITY OF TEXAS
AUSTIN, TEXAS

DESCRIPTION (Adapted from applicant's abstract): Vocalization by anuranamphibians has historically been the subject of intense evolutionary interest because of the fundamental role that sound production plays in materecognition and species isolation. Behavioral ecology of mate attraction

and neural bases for sensory perception have accordingly received considerable attention but mechanisms of sound production are much less studied, even though emitter and receiver are likely to change in a coevolved manner. This research will examine the nature of physical and biological constraints in the evolution of advertisement calls in anuran amphibians. Using a well defined clade of the Neotropical frog genus Physalaemus for which is available a modern molecular phylogeny as well as behavioral assays of female response to conspecific and heterospecific calls, this research will test the hypothesis that evolution of male mating calls proceeds primarily through neurally regulated changes in activation of the laryngeal apparatus rather than by changes in laryngeal morphology. A comparative approach assessing mechanisms and functional morphology of call production within the known phylogeny will permit direct evaluation of this hypothesis. More generally, this analysis will demonstrate the character of biological constraints inherent to the evolution of sexually selected signals in vertebrates.

1F30MH011912-01A1
MARTINI, SHARYL
EXAMINING THE ROLE OF DACHSHUND IN MUSHROOM BODIES
BAYLOR COLLEGE OF MEDICINE
HOUSTON, TEXAS

DESCRIPTION (Adapted from applicant's abstract): The long-term objective of the proposed research is to understand development of the mushroom bodies, structures important for learning and memory in Drosophila melanogaster. Toward this goal, I am studying the function of the novel protein DACHSHUND. Our interest in the dachshund phenotype stems from its abnormal mushroom body structure, although mutant flies also have reduced, roughened eyes and short legs and die shortly after eclosion. Dachshund is the first cloned gene to be associated with mushroom body structural defects. To dissect dachshund's role in mushroom body development, I am proposing three specific aims: (1) Determine if the mushroom body structural defect in dac mutants is cell autonomous. (2) Ascertain when DACHSHUND is required for proper mushroom body formation. (3) Assess dachshund's role in mushroom body fate determination. Dachshund has previously been shown to direct eye formation when ectopically expressed in imaginal discs. The presence of dachshund vertebrate homologs suggests conservation of a molecular and developmental pathway through evolution. If this is indeed the case, studying dachshund's role in mushroom body development could elucidate developmental principles at work in the mammalian brain. Such conservation would not be surprising, since the biochemical pathways involved in learning have been conserved from Aplysia to Drosophila to mammals. If a developmental pathway for structures involved in learning has also been conserved, studying dachshund may help us understand cognitive deficits in humans.

1F32MH011992-01A1
MC CABE, KRISTEN
MENTAL HEALTH SERVICES FOR LATINO CHILDREN
CHILDREN'S HOSPITAL RESEARCH CENTER
SAND DIEGO, CALIFORNIA

DESCRIPTION (Applicant's abstract): The proposed project will provide broad training in mental health services research, with a focus on delivery of culturally effective services to Latino children and families. Substantial literature documents that Latino adults underutilize mental health services despite a need for services that is as great or greater than that of Caucasians. However, we have little information about whether or not the

delivery of mental health services to Latino children parallels this pattern. Further, Latinos appear to be most likely to underutilize outpatient mental health services as opposed to other types of services, such as inpatient mental health. Little is known about barriers to access to outpatient services and the client and therapist factors that contribute to treatment attendance and outcome in an outpatient selling. The proposed research has the following aims: Aim 1: To closely examine barriers to access to services for Latino children with mental health problems. This will be accomplished by interviewing a subsample of Latino families who have children with clinically significant levels of psychological symptomotology and who have or have not sought mental health services, in order to identify barriers to service utilization. Aim 2: Given that specialty outpatient mental health services appear to be the service most underutilized by Latino adults, a pilot study will be conducted to closely examine variables that affect treatment attendance and outcomes for children who seek specialty outpatient mental health services. This will be accomplished through collaboration with Children's Outpatient Psychiatry, a community mental health center that serves a large Latino population.

5F31MH011845-02
MC CARTY, CAROLYN
AFFECTIVE ATTITUDES--MOTHERS OF CLINIC REFERRED CHILDREN
UNIVERSITY OF CALIFORNIA
LOS ANGELES, CALIFORNIA

DESCRIPTION (Adapted from applicant's abstract): A broad base of literature has shown that studying how parents feel about their children--their affective attitudes--can enrich our understanding of adult psychopathology and its course. For example, parents' critical or emotional overinvolved attitudes are known risk factors for relapse among recovering psychiatric patients (Vaughn & Leff, 1976; Hooley, Orley & Teasdale, 1986). Now there is early evidence (e.g., Stubbe et al., 1993) that studying affective attitudes may also enrich our understanding of child psychopathology. Expressed emotion (EE) is the most widely used measure of affective attitudes employed in research on the family environment as it relates to psychopathology. Most of this work has been conducted with adult populations. To assess the potential of maternal EE to enrich our understanding of child psychopathology, the proposed research aims to assess its relation to such key child and family variables as (1) symptom patterns, (2) maternal psychopathology, (3) parent-child interactions, (4) children's own EE and (5) demographic characteristics, using a clinic-referred sample of children and their mothers. Approximately 350 children and their mothers, drawn from 9 community mental health clinics, will be interviewed for the project. Children and their mothers will be administered structured diagnostic interviews, standard questionnaires, a standardized speech sample measure of affective attitudes, and will participate in a conflict interaction task. Structural equation modeling will be used to test an overall model of affective attitudes as well as mediators, moderators, and specific components of the model. This research is a preliminary step toward further studies on EE and child outcome in clinical populations.

5F30MH011221-03
MC KERNAN, MARGARET
NEUROSCIENCE--AMYGDALA AND FEAR CONDITIONING
UNIVERSITY OF TEXAS MEDICAL BR GALVESTON
GALVESTON, TEXAS

DESCRIPTION (Adapted from applicant's abstract): The amygdala is widely believed to play an essential role in the attachment of emotional significance to learning and memory (LeDoux, 1994). The predominant excitatory neurotransmitter in the amygdala is glutamate, and an important, though less extensively studied, subtype of glutamate receptor is the ionotropic AMPA receptor (McDonald et al, 1989). The overall objective of this proposal is to characterize the native AMPA receptors in the amygdala by determining the electrophysiological properties of these receptors and correlating these properties with the specific receptor subunit composition (GluR1-4). Specific Aim #1 will be to characterize the electrophysiology of AMPA receptors in the lateral amygdala nucleus via whole-cell patch clamp recording from both amygdala slices and dissociated cells. Specific Aim #2 will be to determine the receptor subunit composition of the same neurons characterized in S.A. #1 by the techniques of antisense RNA amplification and double-labeling with biocytin and GluR antibodies and correlate this with the electrophysiological data to determine the functional contribution of each subunit in native tissue. Specific Aim #3 will analyze the role of AMPA receptors in the lateral amygdala in the expression of fear and anxiety by examining fear conditioning, a animal behavioral correlate of anxiety in humans; an attempt will be made to elucidate the underlying synaptic changes which accompany this emotion-based learning. Ultimately, these experiments will increase the understanding of the circuitry underlying fear and anxiety and provide insight into therapeutic avenues for the treatment of human anxiety disorders, which represent a widespread and difficult challenge to the mental health community.

1F31MH012183-01
MCAULIFFE, SEAN
MULTIPLE REPRESENTATIONS OF OBJECT SHAPE
UNIVERSITY OF CALIFORNIA
LOS ANGELES, CALIFORNIA

DESCRIPTION (Applicant's Abstract): The proposed research will investigate the representations of shape that permit us to recognize objects at multiple levels of abstraction. I hypothesize that a primary representation-which is a categorical description of an object's parts and their interrelations-provides abstract and relatively view-invariant information that is useful for determining an object's general class (e.g. a car) and that a secondary representation-which is a more viewpoint-sensitive (and perhaps view-based) metrically-rich representation-provides a basis for determining an object s specific identify (e.g. "my" car). The proposed research will contribute to the growing body of findings supporting the notion of multiple, integrated representation of shape for object recognition. Moreover, the proposed research will introduce a new experimental method for identifying these primary and secondary representations.
The proposed research introduces a new framework for studying object recognition at multiple levels of abstraction. Our ability to recognize objects at multiple levels of abstraction is centrally important: recognizing objects as members of a general class but not distinguishing individual instances would be decidedly maladaptive; and recognizing instances out failing to appreciate that different instances may nonetheless belong to a common class would be equally maladaptive. In spite of the importance of our capacity to recognize objects at multiple levels of abstraction, this capacity is currently not will understood, either empirically or theoretically. The results of the proposed experiments will contribute to our understanding of this important capacity, and place important constraints on theories of human object recognition.

5F31MH011661-03
MCFARLAND, NIKOLAUS
THALAMOSTRIATAL PROJECTION--A DIRECT FEEDBACK LOOP
UNIVERSITY OF ROCHESTER
ROCHESTER, NEW YORK

The objective of the proposed research is to examine the relationship between thalamic and cortical inputs to the striatum from areas which receive basal ganglia output. The striatum functions as the main input nucleus of the basal ganglia and receives inputs primarily from the cerebral cortex, the thalamus and the midbrain. The thalamus provides the second largest source of input to the striatum. In the primate, the striatum receives massive inputs primarily from the "non-specific" thalamic nuclei, including the midline and intralaminar nuclei. Some studies have also suggested that the "specific" thalamic nuclei, including the ventral anterior and ventral lateral nuclei, have significant projections to the striatum in the monkey. The ventral anterior and ventral lateral nuclei receive the bulk of basal ganglia output from the basal ganglia and are primarily thought to relay this information to the cortex. The existence of thalamostriatal projections from the ventral anterior and ventral lateral nuclei suggests that the basal ganglia receives a direct feedback from the thalamus. As loss of function in basal ganglia circuits is associated with several neurologic disorders including Parkinson's disease and Huntington's disease and psychiatric disorders such as schizophrenia, how the thalamic input affects striatal output neurons and its relation to both the excitatory input from the cortex and the dopaminergic input from the midbrain may be crucial to understanding the pathophysiology of some of these disorders. The proposed experiments explore the organization of the thalamostriatal projections from the ventral nuclei and their relation to corticostriatal inputs from areas which also receive basal ganglia output.

1F31MH012120-01
MCGAVERN, DORIAN
CELLULAR IMMUNE RESPONSE AND NEURAL DYSFUNCTION
MAYO FOUNDATION
ROCHESTER, MINNESOTA

DESCRIPTION (Applicant's Abstract): The candidate requests 3 years of predoctoral support to get training in the fields of molecular biology, immunology, and neuroscience as they relate to his studies of the interactions between immunologic effectors and the CNS following the induction of a chronic inflammatory response. The long term objective of this research project is to implicate components of the cellular immune response in the disruption of neural function following the induction of a chronic inflammatory response in the central nervous system (CNS). This research is relevant to both mental health and chronic immune-mediated diseases, as it is based on the premise that multiple etiologic factors function through a common pathway to disrupt neural function. The common pathway is the induction of a chronic CNS inflammatory response. The research will characterize axonal areas, neuronal cell number, spinal cord atrophy, and sodium channel distributions following the induction of a chronic CNS inflammatory response in mice deficient in various immunologic effectors. The first aim addresses the role of the class I- and class II-mediated immune response in the disruption of axons, neurons, and sodium channel distributions, while specific aim two focuses on the cytotoxic T

cell effectors: perforin, fas, fas ligand, and IFN-g. Characterization of axons, neurons, and sodium channels will serve as a sensitive marker of CNS disruption. It is hypothesized that mice deficient in immunologic effectors necessary for the induction of neural dysfunction will have preserved axons and spinal cord areas, as well as increased sodium channel densities in the spinal cord white matter. Furthermore, identification of immunologic effectors that are detrimental to neural function during a persistent CNS inflammatory response could lead to possible therapeutic interventions.

1F31MH011846-01
MCISAAC, HEATHER
PROSPECTIVE MEMORY IN NORMAL AND ABNORMAL AGING
UNIVERSITY OF BRITISH COLUMBIA
VANCOUVER, CANADA

DESCRIPTION (Adapted from applicant's abstract): The broad long-term objective of the proposed research is to learn about prospective memory and its relationship to other cognitive systems such as attention, perception, and especially retrospective memory. Prospective memory has received little attention from memory researchers in contrast to retrospective memory which has received little attention from memory researchers in contrast to retrospective memory which has been extensively studied. In some sense, prospective memory--remembering to carry out plans in the future--can be thought of as the logical complement of retrospective memory--remembering previously learned information, but even though we have an extensive framework for thinking about retrospective memory (e.g., short-term memory, procedural/episodic/semantic memory), such a framework has not yet been developed for prospective memory. The first aim of the proposed research is to construct a framework for categorizing prospective memory tasks. The second aim is to validate this framework by means of the existing literature on prospective memory. The third aim is to test core predictions of this framework by means of new experimental work, which will focus primarily on age-related change in prospective memory. The proposal makes use of a lifespan approach, a design that allows for continuous sampling across ages so that the data will be suitable for quantitative modeling techniques. Additionally, frontal lobe and Alzheimer's patients will be included to learn more about the break-down of the specific components of prospective memory and the neural architecture which supports this memory function. The proposed research on prospective memory will give insight into age-related cognitive decline and cognitive dysfunction in patients affected by accident or disease.

5F32MH011259-02
MCKAY, SHAREN
NEUROTROPHIC FACTORS AND NEURAL PLASTICITY IN APLYSIA
YALE UNIVERSITY
NEW HAVEN, CONNECTICUT

DESCRIPTION (Adapted from Applicant's Abstract):
Many similarities exist between neural plasticity during development and the plasticity associated with learning and memory in the adult. The mollusc Aplysia provides an excellent model system for studying the mechanisms of development and learning in parallel. Recent work has revealed that neurotrophic factors, traditionally studied with respect to developmental plasticity, may play a role in adult organisms during learning and memory. The goal of the proposed research is to study the role of neurotrophic factors in Aplysia in the process of long-term

synaptic facilitation of the neurons underlying defensive withdrawal reflexes. Using the Aplysia model it will be possible to determine when and how neurotrophic factors work in modulating synaptic response and then compare these forms of modulation with the actions of growth factors in development in the same experimental system.

1F31MH012059-01
MCKOWN, CLARK
CHILDRENS DIFFERENTIAL RESPONSE TO TEACHER EXPECTATIONS
UNIVERSITY OF CALIFORNIA
BERKELEY, CALIFORNIA

DESCRIPTION (Adapted from applicant's abstract): Teacher expectations can influence children's psychosocial outcomes; yet not all children confirm teacher expectations. Social psychology and developmental psychopathology offer theories to help predict which children are susceptible to teacher expectations and which children resist those expectations. To date, however, almost no empirical research has tested these predictions. In addition, very few researchers have examine children's differential response to high and low expectations (controlling for prior achievement). The proposed research applies what is known about expectancy process, stereotype threat, and self-verification to make and test predictions about children's differential susceptibility to expectancy effects. In particular, this research will evaluate the influence of ethnicity, gender, and self-concept in first, third, and fifth grade children's differential response to teacher expectations. Unlike previous research, the proposed project explores children's differential response to high and low expectations separately. This research also explores developmental changes in children's differential response to teacher expectations.

5F32MH011403-02
MCMANIS, MARK
CHILDREN'S TEMPERAMENT AND EMOTIONAL REACTIVITY
HARVARD UNIVERSITY
BOSTON, MASSCHUSETTS

DESCRIPTION (Adapted from Applicant's Abstract):
The research proposed here seeks to combine two diverse methodologies that have been used to study emotional phenomenon. There is a growing corpus of research from animal and human studies linking the startle to affective states. There is also a large body of research on children who show extreme levels of behavioral inhibition when presented novel stimuli, indicating that there are neurophysiological differences that set them apart from their uninhibited peers. The proposed studies investigate how neurophysiological indices of behavioral inhibition, such as heart rate variability, may also index differences in affective picture processing, as measured using the startle probe. The first study proposed examines responses in children who show differences in heart rate variability as a function of their classification as either inhibited of uninhibited. The second study using the startle probe methodology to investigate children's individual differences in affective picture processing. Pleasant, neutral, and unpleasant pictures will be shown to inhibited and uninhibited children and startle probes will be delivered during picture viewing. Startle responses will be used to determine affective processing in the children. The third study extends the work done in the second study to include anticipatory anxiety. Inhibited and uninhibited children will get startle probes while awaiting a warned aversive event. A noise blast will be given to

participants 20 seconds after a warning tone. During that waiting period a startle probe will be delivered and the size of the participant's response will be used to determine affective state.

5F31MH011826-02
MILLER, DAVID
NMDA RECEPTOR FUNCTION IN NEUROCHEMISTRY OF PARKINSONISM
RUTGERS THE STATE UNIV NEWARK
NEWARK, NEW JERSEY

DESCRIPTION (Adapted from applicant’s abstract): A hyperglutamatergic state secondary to DA loss has been suggested to exist in PD. By examining the effects of treating both neurochemical pathologies (DA degeneration and hyperglutamatergic activity) of this disease, the results of experiments described herein will contribute relevant and necessary neurochemical data to a body of literature suggesting that NMDA receptor blockade has anti-Parkinsonian effects. Proposed studies will examine the role of this glutamate receptor subtype in the neurochemistry of intact and DA-denervated striatum. In vivo microdialysis and high performance liquid chromatography with electrochemical detection will be used to monitor striatal extracellular DA and ACh in freely-moving rats. Unilateral 6-hydroxydopamine (6-OHDA) lesions will serve as an animal model of PD. L-DOPA, the precursor of DA, is the most effective means for reversing PD symptoms, except after chronic administration, at which point deleterious behavioral side-effects arise.

This effect of chronic L-DOPA is thought to be due to the lack of a neurochemical balance in striatum which is important for the processing of sensorimotor information by the basal ganglia. Experiments in this proposal will test the ability of MK-801, a non-competitive NMDA receptor antagonist, and L-DOPA to collectively restore the balance between DA and ACh (an index of excitatory drive to striatum) in the DA-denervated striatum. Conclusions from these studies will provide insight to the neurochemical etiology of PD and also to the potential viability of NMDA receptor antagonism in the treatment of this disease.

1F32MH012141-01
MINER, LEEANN
MONOAMINE INTERACTIONS IN THE PREFRONTAL CORTEX
UNIVERSITY OF PITTSBURGH
PITTSBURGH, PENNSYLVANIA

DESCRIPTION (Applicant's Abstract): The midbrain dopamine (DA) neurons that project to the prefrontal cortex (PFC) are critical for normal cognitive functioning. Consequently, the cognitive dysfunctions observed in schizophrenia have been partially attributed to the diminished amount of DA input to the PFC of patients with this disorder. However, the regulation of DA transmission within the PFC is not only determined by the activity of the DA neurons but also by the levels of the other monoamines, norepinephrine (NE) and serotonin (5-HT), within that area. This is evident in studies showing the importance of NE terminals in removing DA from the extracellullar space within the PFC and the importance of DA and 5-HT blockade in the therapeutic efficacy of most atypical antipsychotics. In order to understand better the nature of the interactions between the monoamines within the PFC, dual-labeling immunocytochemistry and electron microscopy will be used to determine 1) whether there are direct structural bases for interactions between DA terminals and terminals containing NE or 5-HT, and 2) whether there are morphological substrates for modulation of DA

neurotransrnission within the PFC by the transporters for NE and 5-HT. These anatomical studies revealing the relationship of the monoamine innervation of the PFC will contribute to our current knowledge of the organization and function of this complex area, and thereby assist in the development of more efficient therapeutic tools for disorders of PFC function, such as schizophrenia.

1F30MH012045-01
MORGAN, PETER
PEPTIDERGIC MODULATION OF A CENTRAL PATTERN GENERATOR
MOUNT SINAI SCHOOL OF MEDICINE OF CUNY
NEW YORK, NEW YORK

DESCRIPTION (Adapted from applicant's abstract): Due to the crucial role that rhythmic behaviors play in human interaction with the environment, the neural networks that generate rhythmic motor output have been extensively investigated. These networks were named central pattern generators (CPGs) because they can generate rhythmic motor outputs even in the absence of patterned sensory inputs of any type. The complex synaptic interconnectivity and active biophysical properties of CPG neurons endow these circuits with the ability to generate a multitude of motor patterns that match the behavioral output to the situational demands of the environment. It has been hypothesized, but not proven, that the selection of specific motor patterns is implemented by the action of neuromodulators that are released in response to specific configurations of stimuli. The aim of the research proposed in this application is to test this hypothesis in a simple model system in which specific modulator-containing neurons can be identified and studied while the behavior of the organism is monitored. A combination of electrophysiological, biochemical, immunocytological, and behavioral techniques will be applied to provide a well-integrated set of answers.

5F32MH011105-03
MULVANEY, JENNIFER
BIOPHYSICAL ANALYSIS OF A NOVEL NON-NMDA CHANNEL
CORNELL UNIVERSITY
ITHACA, NEW YORK

DESCRIPTION (Adapted from applicant's abstract): Excitatory amino acid receptors (EAA) are believed to be the predominant receptors mediating fast excitatory neurotransmission in the vertebrate central nervous system and have been linked to synaptic plasticity and learning. The proposed studies will focus on the class of EAA receptors that are insensitive to N-methyl-D-aspartate (NMDA), known as nonNMDA receptors. Functional characterization of nonNMDA receptors has been difficult because nonNMDA receptors have complex pharmacological sensitivities and diverse molecular subunits. Specifically, this project involves the biophysical and pharmacological characterization of a novel ibotenate-activated nonNMDA receptor/channel that has two unusual characteristics, it is permeable to Ca2+, and its open probability (Po) appears to be sensitive to extracellular Ca2+ concentration. Whole cell and single channel recording techniques will be used to analyze the effects of Ca2+ on the Po of the channel as well as to investigate the site of Ca2+ modulation. Single-cell molecular biology techniques will be used to investigate probable subunits which may form the ibotenate-activated channel and to provide information towards proposing a model of likely subunit composition. Results from the proposed research will provide significant new information concerning the structure/function of a particular ibotenate-

activated nonNMDA receptor/channel and an understanding of the role(s) this receptor/channel subtype may play in excitatory neurotransmission in vertebrate brain.

5F31MH011470-02
MYERS, SCOTT
MECHANISMS OF RAT GLUR2 GENE EXPRESSION IN NEURONS
EMORY UNIVERSITY
ATLANTA, GEORGIA

DESCRIPTION (Adapted from applicant's abstract): A growing body of literature shows that GluR2 mRNA levels are down-regulated in specific neurons following epileptiform-like activity and global is chemia in rats. The selective loss ofGluR2 in neurons would favor enhanced calcium entry via AMPA receptors into these cells and could exacerbate or initiate local excitotoxicity, sincere combinant AMPA receptors lacking a GluR2 subunit exhibit high calcium permeability. For this reason we are interested in exploring specifically how neurons regulate expression of this key subunit. The primary focus of this proposal is to identify the critical regulatory elements in the GluR2 promoter that control GluR2 expression in neurons. We have subcloned and sequenced the 5'-flanking region of the rat GluR2 gene and have identified multiple regions governing GluR2 expression in neurons. Based on our preliminary data, we propose that the GluR2 promoter contains both a positive, neuron-specific enhancer region that promotes expression in neurons, as well as a neuron-specific silencer region that represses GluR2 expression in non-neuronal cells. We hypothesize that changes in the expression of the transcription factors that recognize these regulatory sites may lead to changes in GluR2 levels that exacerbate or initiate excitotoxicity. The long-term goal of these experiments is to develop a new strategy for stroke therapy based on preventing the loss of the GluR2 subunit.

1F31MH011968-01A1
NAIR, HEMANTH
BRAIN IMAGING OF DEVELOPMENTAL LEARNING EFFECTS
UNIVERSITY OF TEXAS
AUSTIN, TEXAS

DESCRIPTION (Adapted from applicant's abstract): The aim of the proposed research is to combine brain metabolic mapping and structural equation modeling, a statistical path analysis technique, to study postnatal maturation of the functional interactions of neural systems related to reinforcement, memory, and behavioral inhibition in the preweanling rat. In the proposed experiment, preweanling pups at 16-17 and 11-12 days of age will be trained, in a straight alley runway, on two reward schedules, patterned single alternation (PSA) and random partial reinforcement (PRF). Following training on these schedules, animals will be injected with fluorodeoexyglucose (FDG), a radio labeled glucose analog and then given 50 trials of extinction training, i.e. continuous non-reward. Immediately following training, they will be sacrificed and their brains processed for FDG. Glucose utilization in a number of brain regions will be quantified using image analysis sofware. Structural equation modeling will be applied to these data to quantify functional influences between anatomically connected brain regions. The network models derived from this process from PSA and PRF groups at each age will be compared. PSA and PRF comparisons in the 16-17 day old age group should reveal functional differences in the coordinated function of brain regions between animals demonstrating behavioral inhibition and perserveration, respectively. Comparison of 16-17

day old PSA and PRF groups to their 11-12 day old counterparts should reveal ontogenetic differences in brain activity related to the behavioral differences across the two ages. Handled controls will be included to control for brain activation related to handling and not learning per se. The major goal of this work is to contribute substantially to the understanding of metabolic maturation of brain regions related to reinforcement, memory, and behavioral inhibition, and how changes in their coordinated activity during postnatal development are reflected in behavior.

1F30MH011986-01A1
NAKAMURA, KEN
GLUTATHIONE AND DOPAMINERGIC NEURONAL SURVIVAL
UNIVERSITY OF CHICAGO
CHICAGO, ILLINOIS

DESCRIPTION (Adapted from applicant's abstract): An increased production of reactive oxygen species is thought to be critical to the pathogenesis of Parkinson's disease. Furthermore, a growing body of evidence indicates that alterations in the glutathione system, and specifically the detoxification of hydrogen peroxide by glutathione peroxidase (GPx), may play a central role in the development of this oxidative stress. In this study, we will use GPx knockout (GPxKO) mice and recombinant adenoviruses to examine the significance of GPx and glutathione (GSH) to the survival of dopaminergic neurons. In addition, we will investigate how adding the putative exogenous source of free radical 1-methyl-4-phenylpyridine affects the role of GPx in handling oxidative stress in dopaminergic neurons. We will begin by examining the survival of dopaminergic neurons in dissociated mesencephalic cultures which are designed to minimize glial contamination. In addition, we will use digital imaging microfluorimetry to measure levels of free radicals and GSH in individual dopaminergic and nondopaminergic neurons. Subsequently, we will use an in vivo paradigm to study the GSH system in a more physiologic environment.

1F31MH012106-01
NEMANIC, SARAH
ANIMAL VISUAL, SPATIAL, AND CONTEXTUAL LEARNING/MEMORY
UNIVERSITY OF TEXAS HLTH SCI CTR HOUSTON
HOUSTON, TEXAS

DESCRIPTION (Adapted from applicant's abstract): The proposed research will use selective lesion techniques to assess the role of the hippocampal formation, perirhinal cortex and parahippocampal gyrus (TH/TF) in recognition memory in rhesus monkeys. Specifically, ibotenic acid lesions of the hippocampal formation will be compared to aspiration lesions of the perirhinal cortex and parahippocampal gyrus (TH/TF) on newly designed behavioral tasks. The visual recognition tasks, delayed nonmatching-to-sample and preferential looking will be used to test the effects of these lesions on spatial recognition memory and on contextual recognition memory. For spatial recognition, in both tasks, the monkeys will be required to respond (touch or look at, respectively) a new location on the screen. For contextual recognition, in both tasks, the monkeys will be required to respond to the new object when the context in which the object is learned has been changed. Results from these experiments will permit elucidation of the respective contributions of the hippocampal formation, perirhinal cortex and parahippocampal gyrus (TH/TF) in spatial and contextual recognition memory.

1F31MH012421-01
NETOFF, THEODEN
DEFECTING GENERALIZED SYNCHRONY OF CELLS IN HIPPOCAMPUS
GEORGE MASON UNIVERSITY
FAIRFAX, VIRGINIA

DESCRIPTION (Adapted from Applicant's Abstract):
Cells in the nervous system are often highly interconnected; however, their firing times are synchronized during certain events such as gamma oscillations and theta oscillations. During these oscillations, crosscorrelations can show synchronization of spike times. However, when the cells are not synchronized, it is our hypothesis that there may be more complex interactions, such as generalized synchrony, that cannot be detected using linear analysis (i.e. cross correlation). These interactions may give a much richer understanding of the interactions between cells. Currently, no technique exists to detect these complex interactions in neurons. We intend to record from two pyramidal cells in the hippocampus simultaneously with and without glutamate antagonists. The glutamate antagonists increases synchrony between cells. Analysis to detect nonlinear functional relations between the firing patterns of the cells will be applied to the time series. We will use a technique called mutual prediction. It has been used to show interactions between single cells and the population activity in the stimulated cat spinal cord that linear techniques could not detect. This work will also develop a new technique for detecting nonlinear interactions by comparing patterns of interspike intervals using unstable periodic orbits. If a functional relationship is found between the spontaneous firing pattern of two cells when they are spontaneously firing, these techniques will be used, in a collaboration with another laboratory, to analyze interactions between two cells in the olfactory bulb and how they are effected by different odorants.

5F30MH011391-03
NETT, SHOLEEN
SEXUAL DIMORPHISM IN HYPOTHALAMIC SYNAPTIC TRANSMISSION
DARTMOUTH COLLEGE
HANOVER, NEW HAMPSHIRE

DESCRIPTION (Adapted from applicant's abstract): The long term goal of this thesis project will be to determine the role of specific types of gamma-aminobutyric acid type A (GABA-A) receptors in the mammalian hypothalamus in mediating the expression of gender-specific sexual behaviors. It has been experimentally established that gonadal steroids act during a perinatal critical period to induce morphological differences in the mammalian brain which provide the basis for gender-specific sexual behaviors. Within the hypothalamus, it has been shown that specific nuclei, namely the ventromedialnucleus (VMN) and the preoptic area (POA), play essential roles in the expression of these behaviors in adult rats. Specifically, it is believed that activity within the VMN facilities female sexual behaviors where as activity within the POA inhibits female sexual behaviors and is critical for transmission in these areas has been implicated in the control of adult sexual behavior and data from our laboratory suggests that significant gender-dependent differences in GABA-A receptor function are found between VMN neurons in female versus male neonatal rats. The specific goals of this project will be to determine if these gender-specific differences in GABA-A receptor properties are regulated by exposure to steroids during development and if these differences in function lead to different patterns of synaptic

transmission in the female versus male hypothalamus which then contribute to the expression of appropriate behaviors.

1F32MH011957-01
NOELLE, DAVID
NEUROCOMPUTATION OF EXPLICIT LEARNING FROM INSTRUCTION
CARNEGIE-MELLON UNIVERSITY
PITTSBURGH, PENNSYLVANIA

DESCRIPTION: (Applicant's Abstract): Humans employ a wide array of strategies when learning to perform a task. Connectionist learning models, however, have typically focused on only a single learning strategy - on the slow induction of regularities from direct experience with a task domain. While these models succeed at explaining many phenomena, they fail to capture a rapid learning which results when explicit methods are used, such as hypothesis testing or relying upon verbal instruction. The research proposed here embarks on a journey towards a unified computation model of human learning - a model which will explain both healthy behavior and the use of compensatory strategies in the face of difficulty or disability. Specifically, a standard connectionist implicit learning mechanism will be augmented with an attractor network model of frontal working memory and a "fast weight" model of medial temporal declarative memory, forming an integrated system capable of both inductive generalization and learning from explicit verbal instruction. This complex model will be tested against human behavior in a number of category learning domains.

1F32MH011857-01A1
OBRIETAN, KARL
ADENYLYL CYCLASES AND CIRDADIAN RHYTHM
UNIVERSITY OF WASHINGTON
SEATTLE, WASHINGTON

DESCRIPTION (Adapted from applicant's abstract): The circadian organization of behavior plays a critical role in an organisms's response to social and light/dark cycles encountered on a daily and seasonal basis. Alterations in the normal function of the mammalian biological clock, located in the suprachiasmatic nucleus (SCN), leads to a variety of neurological abnormalities including sleep disorders, depression, and mental fatigue. A feedback regulator of circadian rhythmicity is the neurohormone melatonin. Changes in environmental light information received by the SCN are converted into the nocturnal synthesis and release of melatonin from the pineal gland. An important regulatory of melatonin synthesis and circadian clock function is cAMP. cAMP regulates the transcription of several proteins critical for the circadian expression of melatonin, including serotonin N-acetyltransferase (NAT), which is responsible for catalyzing the synthesis of melatonin from serotonin. Additionally, cAMP may also play an important role in circadian timekeeping in the SCN by regulating gene transcription. By integrating different intracellular signal transduction pathways, the Ca2+/calmodulin-sensitive adenylyl cyclases may play an important role regulating circadian rhythmicity. With the two unique tools developed in the laboratory of Dr. Storm (mutant mice lacking Ca2+/calmodulin-sensitive adenylyl cyclases and a CRE-lacZ transgenic mouse strain), I propose to elucidate the roles Ca2+/calmodulin-sensitive adenylyl cyclases play in melatonin synthesis and in the modulation of SCN circadian rhythmicity and to determine whether CRE-mediated transcription in the SCN and pineal gland is regulated in a circadian manner.

1F32MH011990-01
OCHSNER, KEVIN
SOCIAL COGNITIVE NEUROSCIENCE APPROACH--RATIONALIZATION
HARVARD UNIVERSITY
BOSTON, MASSCHUSETTS

DESCRIPTION (Applicant's Abstract): This project aims to develop a social cognitive neuroscience approach to understanding the use of rationalization to exert cognitive control over emotion (a) by elucidating which cognitive and affective information processing mechanisms are used to rationalize preferences when making a self-threatening choice among alternatives, and (b) by studying the breakdown of these mechanisms due to brain trauma or aging to help understand their functioning in normal populations. Experiments 1-4 test the hypotheses that rationalization of attitudes takes effort and cognitive resources, evolves over time, may alter both cognitive and affective components of attitudes, and may be so complete as to render revised attitudes as automatically accessible as un-rationalized ones. Experiments 5-7 provide converging evidence in support of these hypotheses using brain damaged patients. Experiment 5 uses amnesics to test the hypothesis that rationalization can occur even when initial attitudes and the reason for changing them (a stressful decision) can't be recalled; Experiment 6 tests the hypothesis that the cognitive resources used to rationalize are being impaired after damage to the frontal lobe; and Experiment 7 tests the hypothesis that damage to brain areas used to evaluate the personal, emotional significance of a choice will limit motivation to rationalize. Experiments 8-11 extend the results of the first four experiments to the elderly to determine whether and how age-related declines in the flexible use of cognitive resources will impair rationalization.

5F31MH011933-02
ORLANDO, LIANNA
METABOTROPIC RECEPTORS AND EFFECTORS IN EXCITOTOXICITY
MASSACHUSETTS GENERAL HOSPITAL
BOSTON, MASSACHUSETTS

DESCRIPTION (Adapted from applicant’s abstract): Glutamate is the major excitatory neurotransmitter in mammalian brain, and excessive activation of glutamate receptors is thought to play a role in many disease processes. Recent data indicates that the G-protein linked mGluRs have effects in many models of excitotoxic damage. In fact, in a rodent model of Huntington’s disease, mGluRs have been shown to have a permissive role in NMDA toxicity. Much evidence implicates the Group I mGluRs. The cell types lost following injection of N-methyl-D-aspartate (NMDA) have more Group I mGluRs than the spared cell types and Group I mGluRs are linked to increases in intracellular Ca2+ and activation of protein kinase C. The latter have both been implicated in many models of excitotoxicity. This proposed project will investigate the hypothesis that Group I mGluRs are involved in excitotoxicity. First, by co-injecting antagonists of the Group I mGluRs with NMDA into the striatum of rats, I will determine if the striatum is protected against NMDA toxicity. Next, second messenger pathways activated by the Group I mGluR splice variants will be determined in clonal cell lines and striatal slices. Third, inhibitors of these pathways will be tested for their ability to block mGluR contribution to striatal NMDA toxicity, downstream of receptor activation.

These experiments will identify which Group I metabotropic glutamate receptor and effector pathways contribute to NMDA excitotoxicity with the hope of

identifying better therapeutic targets for Huntington’s disease and related excitotoxic disorders.

5F32MH011720-02
OTMAKHOVA, NONNA
MECHANISMS OF D1 DOPAMINE ENHANCEMENT OF EARLY LTP
BRANDEIS UNIVERSITY
WALTHAM, MASSACHUSETTS

DESCRIPTION (Adapted from applicant's abstract): The neuromodulator DA is implicated in mechanisms of attention and reinforcement of learning. Many brain disorders (schizophrenia, attention deficit, Parkinson disease, alcohol and drug addiction) involve the disruption of DAergic function, and cause different forms of memory impairment. LTP in the CA1 region of the hippocampus is a convenient model for studies of cellular mechanisms of memory. Our data with field potential recordings indicate that D1 DA modulations enhances early LTP by a cAMP-dependent mechanism. This application deals with the intracellular targets of DA and cAMP action. Two fundamental possibilities for the enhancement of LTP by DA will be addressed: D1 activation could increase depolarization during the tetanus or it could affect the enzymatic mechanisms of plasticity. The first possibility, D1 action on electrical properties of pyramidal cells, will be accessed by whole-cell recording methods (Specific Aim 1). The second possibility, that D1 and cAMP affects the enzymatic machinery of LPT, will be analyzed by voltage clamp with intracellular perfusion of substances of interest (Specific Aim 2).

5F31MH011616-02
PAGE, WILLIAM
NEURONAL RESPONSES TO SELF-MOTION DURING SMOOTH PURSUIT
UNIVERSITY OF ROCHESTER
ROCHESTER, NEW YORK

DESCRIPTION (Adapted from applicant's abstract): While moving through the world, smooth pursuit eye movements are used to maintain fixation on objects of interest. These eye movements can distort the visual motion on the retina thereby complicating visual motion processing. How is spatial orientation maintained during eye movements, and how do we control these pursuit movements in complex visual scenes? Cortical area MST is thought to be implicated in both of these processes because it is known to contain neurons which are activated by large-field visual motion from self-movement (optic flow) and by pursuit eye movements (Duffy and Wurtz 1991a, Komatsu and Wurtz 1987a).The aim is to now record single neuron activity in area MST of monkeys performing a pursuit task during the presentation of visually simulated, and/or real translational, self-motion stimuli. Three aims will be to 1)determine whether the individual neurons are activated both by smooth pursuit and optic flow, 2) characterize the role of retinal and extra retinal signals in these responses, and 3) examine the impact of real translational observer movement (vestibular and somatosensory) on these mechanisms. These experiments will bear on issues of sensorimotor integration for spatial orientation in naturalistic circumstances.

1F31MH011947-01A1
PALADINI, CARLOS
AFFERENT REGULATION OF NIGRAL DOPAMINERGIC NEURONS
RUTGERS THE STATE UNIV NEWARK
NEWARK, NEW JERSEY

DESCRIPTION (Adapted from Applicant's Abstract):
Pathophysiology of the dopaminergic neurons of the substantia nigra pars compacta (SNC) underlies many of the symptoms of neurological disorders such as Parkinson's disease and psychoses such as schizophrenia. These neurons and their synaptic targets also serve as the sites of action of stimulant drugs of abuse such as cocaine and antipsychotic drugs. Dopamine neurons fire in three patterns, namely random, pacemaker, and bursty firing pattern. The different firing patterns, especially the bursty pattern, of the nigrostriatal neurons of the SNC have been correlated with environmental stimuli relevant to reward contingencies. Also spikes of dopaminergic neurons of the SNC clustered in bursts may release more dopamine at synaptic targets than single spikes. The fact that these cells fire differently in vitro than in vivo suggests that the afferent control of these neurons is critically involved in the regulation of their firing pattern. The main hypothesis to be tested in this proposal is that the firing pattern and modulation of dopaminergic neurons is controlled through disinhibition in large part by the GABAergic afferents to these cells using electrophysiological techniques combined with controlled local application of selective antagonists for different receptors. By investigating how receptors on and afferents to dopaminergic neurons affect firing pattern and understanding which receptors mediate the afferent control of these cells, a better understanding can be achieved of how and to what extent dopaminergic neurons are controlled by afferents.

1F32MH011946-01
PARK, JAE
NEUROENDOCRINE REGULATION OF THE CIRCADIAN RHYTHMS
BRANDEIS UNIVERSITY
WALTHAM, MASSACHUSETTS

DESCRIPTION (Adapted from applicant's abstract): The biological timing system is located in the nervous system of a wide variety of animals and consists of an entrainable clock which generates circadian information, which then governs the rhythmic behavior. Alterations of this system profoundly affect the animal's (including human) performance and are closely associated with certain types of affective disorders. Since the signal flow (input to pacemaker to output) for the circadian rhythms is common to most animal species, basic information obtained from research in the fruit fly is intertwined with clinical significance in higher animals. Most molecular genetic studies of the biological timing system in Drosophila have focused on the clock genes period and timeless. In this proposal, consideration is given to neuroendocrine factors that may also affect the fly's pacemaking system. A neuropeptide called pigment-dispersing hormone (PDH) has been known to be involved in the circadian rhythmic changes on integumental color in crustaceans. Similar neuropeptides have been identified, and their biological functions appear related to insect circadian rhythms. Recently, cDNA of the Drosophila PDH homolog (Dm-PDF) has been cloned by the applicant, and the proposed research will extend this initial accomplishment to define the roles of Dm-PDF in the regulation of the fly's biological timing system using comprehensive molecular genetic approaches along with behavioral analyses.

5F30MH011189-04
PATRICK, TODD
ENGINEERED BISPECIFIC ANTIBODY TARGETING OF BRAIN TUMORS
UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN

CHAMPAIGN, ILLINOIS

DESCRIPTION (Adapted from applicant's abstract): Tumor cells have long been known to escape normal immune recognition mechanisms. A possible therapeutic strategy that obviates the need for normal T cell recognition involves the use of bispecific antibodies. Although a number of clinical trials with bispecific antibodies have proceeded, there is much to learn about their optimization in order to take full advantage of them as drugs. The general goal of this proposal is to develop and test, state-of-the-art bispecific antibodies in an animal model for brain cancer. SV40 transgenic mice develop tumors in the brain choroid plexus, and die at a mean age of 104 +/- 12 days. This animal model most resembles the human disease and thus serves as a useful preclinical test of these drugs. The specific goals of the proposed work are: 1) To examine if there is normally, T cell surveillance of brain tumors in the SV40 animal model; 2) To generate monoclonal antibodies to the mouse folate receptors that are present on tumor cells from the SV40 transgenic mice; 3) To engineer, purify, and characterize bispecific antibodies to the T cell receptor and the folate receptor; and 4) To begin to test the in vivo effectiveness of the bispecific antibodies.

5F31MH011589-02
PELLEGRINO, TRISHA
IMMUNOMODULATORY EFFECTS OF SEROTONIN UPTAKE INHIBITORS
GEORGETOWN UNIVERSITY
WASHINGTON, D.C.

DESCRIPTION (Applicant's Abstract): Specific serotonin reputake inhibitors (SSRIs) are the most widely prescribed drugs for treatment of depressive disorders. Preliminary data have shown that acute fluoxetine (FLX) administration significantly suppresses mitogen-induced lymphocyte proliferation and NK cell cytolytic activity. The mechanism and implications of SSRI immune suppression are not yet known. The suppressive effects were found to be dose-dependent, reversible, and selective for serotonin reputake. The lymphocyte effects, but not NK cell effects, appear to be 5HT2A receptor mediated.
These data suggest that SSRI therapy may potentiate the immunosuppression observed in depression, therefore, it is important to characterize the mechanism and effects of acute and chronic treatment with FLX. To test the hypothesis that acute and chronic SSRI treatment suppresses cell-mediated immunity via serotonin receptor activation in normal animals and in animal models of depression, the candidate proposes to determine: 1) the serotonin receptor subtype(s) involved in the acute immunomodulatory effects of FLX; 2) the mechanism/site of action by which acute FLX suppresses immune function; 3) the effects of chronic FLX treatment on immune function in normal animals, and; 4) the effects of acute and chronic FLX in animal model for depression. These studies aim to provide insight into the mechanism of SSRI immunomodulation and the implications they might have on depressed patients receiving SSRI therapy. In addition, these studies aim to increase understanding of the role of endogenous serotonergic systems in modulating the immune response.

5F31MH011344-02
PENNELL, NATHAN
MICROGLIA AND NEURAL TRANSPLANTATION
UNIVERSITY OF FLORIDA
GAINESVILLE, FLORIDA

DESCRIPTION (Adapted from Applicant's Abstract):
Although much research has been done on the characterization and function of transplanted neural tissue, most studies have focused on the neuronal and macroglial elements of the transplant, ignoring a significant group of cells within the central nervous system (CNS), i.e. the microglial cells. The proposed research is designed to address several fundamental questions as to the functional role of microglia within transplanted neural tissue. The hypothesis that microglia, the resident immunocompetent tells of the CNS, are the cellular component most likely responsible for the initiation of immunological rejection of allo- and xenografted neural tissue will be tested. Fetal spinal cord tissue will be depleted of microglia and allografted (using two histo-incompatible rat strains) and xenografted (using two incompatible species) into injured host spinal cords, and the immunogenicity of the transplant assessed, i.e. presence and severity of the host immune response. To complement the depletion experiment, purified suspensions of microglial cells will be allografted into a histoincompatible rat spinal cord in order to test the hypothesis that microglia are capable of initiating a host-derived immune response against the graft. This project differs from previous studies, however, in that the microglia will be indelibly labelled with a genetic marker prior to transplantation, allowing the cells to be identified and traced in the host spinal cord. Furthermore, label led microglia will be transplanted into immunologically tolerant animals, i.e. in which they will not be rejected, in order to test the hypothesis that transplanted microglia have beneficial effects, such as neurotrophic properties and ability to lay down extracellular matrix components. The proposed study should provide a comprehensive examination of the possible beneficial and detrimental roles of microglial cells in neural transplantation, a subject about which very little is known.

1F32MH011949-01A1
PETRULIS, ARAS
PHYSIOLOGY OF INDIVIDUAL DISCRIMINATION/RECOGNITION
BOSTON COLLEGE
BOSTON, MASSACHUSETTS

DESCRIPTION (Adapted from applicant's abstract): The major objective of this proposal is to understand how different olfactory recipient areas of the hamster brain participate in learning and storing odor information about other individual hamsters. This will be done by analyzing the coding properties of single neurons and ensembles of neurons in olfactory cortex, entorhinal cortex and hippocampus while hamsters perform two types of individual discrimination recognition tasks that differ in their processing demands. The first test is a basic habituation discrimination task in which hamsters are repeatedly presented with odors from one individual hamster and are then presented with another animal's odor. Hamsters form and maintain some memory of different individuals' odors over long periods of time as evidenced by habituation of investigation to one odor and increased investigation of the new individual's odor. The second task is a variation on this paradigm in which hamsters are allowed to interact with two individuals (A & B) for several days and are then habituated to one particular odor from A and then tested with another particular odor from A. Behaviorally, hamsters generalize their habituation to the second odor only if they have previously interacted with that animal, indicating that hamsters associate the two perceptually distinctive odors with each other and that they come to represent the individual hamster. This latter test provides an opportunity to test the hypothesis that the hippocampal system

is involved in the formation of declarative (conscious, relational and flexible) memories, but not procedural (unconscious, inflexible, and limited) memories by predicting that only hippocampal neurons will code this odor-odor relationship. In contrast, social odor memories formed in the first task are non-relational and are therefore not predicted to require hippocampal coding but will be represented in olfactory and entorhinal cortex activity. This proposal is part of a broader research program that uses rodent species as experimental models of human amnesia with the explicit intent of characterizing the neural structures involved in human memory formation.

5F32MH011612-02
PHILLIPS, LYNNETTE
SITE SPECIFIC REGULATION OF IMMUNE FUNCTION IN THE CNS
BRIGHAM AND WOMEN'S HOSPITAL
BOSTON, MASSACHUSETTS

DESCRIPTION (Adapted from Applicant's Abstract):
The proposed experiments are based on the hypothesis that distinct neuroanatomical regions of the CNS of the rat will regulate immune cells differently in vivo, depending on the local profile of neurochemicals. Specifically, two major aspects of the cell-mediated immune response which are enhanced following interferon-gamma) injection - T cell traffic and MHC expression - are proposed to be differentially regulated by local CNS environments. Here, these aspects of immune function following INFO-gamma injection in the following regions: (1) the nucleus of the solitary tract (NTS), a brainstem region with primarily inhibitory neurochemicals, (2) the hippocampus, an area containing mainly excitatory neurotransmitters, and (3) the hypothalamus, a region with an abundance of neurohormones. The regulatory environments of the hippocampus and the hypothalamus are proposed to suppress T cell traffic and/or MHC expression, while enhancement of these parameters is expected to occur in the NTS. Pharmacological antagonists against specific neurochemicals will then be used to attribute differential regulation of immune function to major neurotransmitters. Finally, lesion formation after induction of experimental allergic encephalomyelitis, an animal model of multiple sclerosis, will be examined in these neuroanatomical regions to determine if pharmacological manipulation of neurotransmitters affects inflammation. The proposed studies will add insight into the factors that regulate the immune response to antigen in the CNS.

5F30MH011838-02
PIEPER, ANDREW
IN VIVO MODULATION OF THE IP3R BY PHOSPHORYLATION
JOHNS HOPKINS UNIVERSITY
BALTIMORE, MARYLAND

DESCRIPTION (Adapted from applicant's abstract): The phosphoinositide (PI) and adenosine-3',5'-cyclic monophosphate (cAMP) systems are major second messenger pathways involved in a wide array of cellular functions in peripheral tissues and brain. These pathways appear to be important in many psychiatric disorders. Psychoactive drugs, such as lithium, directly affect the PI cycle, and disturbances in cAMP production have been observed in schizophrenic patients. The active mediator of the PI system, IP3, regulates intracellular levels of calcium through binding to its specific inositol 1,4,5-triphosphate receptor (IP3R) on the endoplasmic reticulum. cAMP, also a second messenger, executes myriad physiological effects through activation of

cAMP-dependent protein kinase (PKA). IP3R is phosphorylated in vitro by PKA, which alters its calcium release kinetics. This in vitro observation suggests that the cAMP and IP3 pathways interact. To assess the physiological relevance of this interaction, it is important to demonstrate IP3R phosphorylation in vivo. This application outlines investigation of the regulation and functional consequences of in vivo IP3R phosphorylation at the sites of in vitro PKA phosphorylation. Phosphorylation will be monitored in vivo in rat brain with phosphate-specific antibodies to the IP3R. Consequences of phosphorylation on calcium release kinetics will be determined through 45CA2+-flux assays with both normal receptor and IP3R mutated at the sites of PKA phosphorylation.

5F31MH011868-02
PIERCHALA, BRIAN
RETROGRADE NEUROTROPHIN SIGNALING
JOHNS HOPKINS UNIVERSITY
BALTIMORE, MARYLAND

DESCRIPTION (Adapted from applicant's abstract): Many neuronal populations depend upon trophic molecules supplied by the target cells they innervate for survival and growth during development. The prototypical target-derived neurotrophic molecule, nerve growth factor (NGF), is a member of a family of related molecules called the neurotrophins. NGF promotes growth and survival of sympathetic and some populations of sensory neurons. Because NGF is a target-derived factor, it interacts with receptors on the nerve terminal that must transduce a signal retrogradely to influence biochemical events in the cell body. However, the nature of the retrograde signal propagated from the nerve terminal to the cell body is unclear. We have elaborated upon a compartmentalized culture system utilizing sympathetic neurons developed by R.Campenot in which we can stimulate nerve terminals with NGF and subsequently monitor biochemical responses in single neuronal nuclei. Using this system we have been able to demonstrate that NGF applied to nerve terminals induces phosphorylation of the transcription factor CREB on its transcriptional regulatory site, Ser-133. We propose, in three specific aims, to further investigate whether terminally applied NGF activates transcription of genes that are critical for the sympathetic neuron phenotype, which NGF receptors present on nerve terminals are necessary for retrograde signaling to occur, and what the retrograde signal is by examining molecular and kinetic aspects of it. A better understanding of how neurotrophins signal in a retrograde fashion could provide important therapeutic insight into neurological disorders involving selective losses of neurotrophin-dependent neurons such as the basal forebrain cholinergic pathway, which rapidly degenerates in Alzheimer's disease, as well as developmental abnormalities that are thought to underlie some psychiatric disorders.

1F31MH011777-01A1
PIETRAS, CYNTHIA
HUMAN CHOICE IN SITUATIONS OF UNCERTAINTY AND RISK
UNIVERSITY OF FLORIDA
GAINESVILLE, FLORIDA

DESCRIPTION (adapted from applicant's abstract): The purpose of the proposed research is to investigate human performance in situations of uncertainty and risk. Previous research has found that humans are risk averse when given few choices between certain and probabilistic hypothetical outcomes. These findings appear inconsistent with the many real-world examples of humans risk taking, and with much non-human risky-choice

research. Direct comparisons between human and non-human performance are difficult to make, however because the procedures used to study human and non-human risky choice vary substantially from one another. A primary aim of this research is to examine human risky choice under conditions that are more comparable to those used with non-humans to further investigate some of these discrepancies and to provide additional information in areas wherein no comparable data exist. Two series of experiments will investigate how different kinds of outcomes (real vs. hypothetical, amount vs. delays, and gains vs. losses) and changes in one type of motivational variable (energy budget or aspiration level) influence risk taking. These experiments will also evaluate two models of risky choice, prospect theory from cognitive psychology and the energy-budget rule from behavioral ecology. This research, besides being relevant to cognitive, behavior analytic, and ecological models of choice, may reveal processes useful for understanding humans behavior in situations involving health and safety risks as well as gambling and economic issues.

5F31MH010963-03
PLAUTZ, ERIK
LEARNING-DEPENDENT ALTERATIONS IN PRIMATE MOTOR CORTEX
UNIVERSITY OF TEXAS HLTH SCI CTR
HOUSTON, TEXAS

DESCRIPTION (Adapted from applicant's abstract): Relationships between the functional plasticity of cortical representations and the acquisition and retention of new motor skills in the primary motor cortex of adult primates will be examined using modern neurophysiological and behavioral training techniques. Specifically, the respective roles of increased motor use and increased motor skill on the alterability of sensory and motor representational maps in area 4 will be assessed by comparing pre-training representations with post-training representations. In addition, the role of different classes of sensory input to area 4 on motor topography and alterability will be examined by evaluating differences between rostral and caudal subregions of primary motor cortex.
This research will help clarity the neural mechanisms responsible for the vast array of manual abilities and capacity for motor learning exhibited by higher animals. From a clinical perspective, an understanding of the motor cortex has the potential for providing a model for examining the neurophysiological bases of recovery of motor function following brain damage.

1F31MH012175-01
POWELL, SUSAN
STRESS RESPONSIVENESS IN ABNORMAL REPETITIVE BEHAVIOR
UNIVERSITY OF FLORIDA
GAINESVILLE, FLORIDA

DESCRIPTION: The current training proposal is part of a larger project investigating the development and neurobiological basis of spontaneous stereotyped behaviors in deer mice. This work represents an animal model of Stereotypic Movement Disorder and thus will be a close complement to our studies of stereotypy and related repetitive behavior disorders in individuals with developmental disabilities. Stress has been assumed to play an important role in the pathogenesis and expression of abnormal repetitive behaviors in various clinical populations as well as animals reared or housed in adverse environmental circumstances. Unfortunately, few data are available to test such an assumption. Thus, the present project will test directly the role of stress in the pathogenesis and expression of

stereotyped behavior. The first approach to this problem will be to assess the effect of increased stress responsiveness on the development of spontaneous stereotypy in deer mice. This involves increasing the stress responsiveness of deer mice through extended maternal separation and assessing the development of stereotyped behavior. The second aim is to assess indices of stress responsiveness in stereotypic and non-stereotypic deer mice. This aim involves assessing stress-induced alterations in HPA axis and dopamine function in both stereotypic and non-stereotypic mice. In order to understand more fully the role that glucocorticoid and dopamine function play in the pathophysiology of stereotypy, glucocorticoid receptor mRNA expression in hippocampus and dopamine transporter densities in dopamine terminal fields will also be compared in stereotypic and non-stereotypic deer mice

5F30MH011546-02
PRABHAKARAN, VIVEK
BASAL GANGLIA AND WORKING MEMORY
STANFORD UNIVERSITY
STANFORD, CALIFORNIA

DESCRIPTION (Adapted from applicant's abstract): There is overwhelming lesion and physiological evidence in animals paralleled by focal lesions and clinical evidence in humans that suggests that the basal ganglia plays a key role in working memory. Paradoxically, imaging studies of working memory have failed to activate the basal ganglia. The investigator has been able to show working memory activation within the basal ganglia. The present proposal builds on this pilot data in a systematic fashion. The goal of this project is to delineate areas within the basal ganglia that are important for working memory and to characterize this activation within a psychological construct. Two different aims will be followed to achieve this goal. The set of experiments proposed under Specific Aim 1 will utilize fMRl in order to identify neuralsubstrates within the basal ganglia that are specific to different domains of working memory. If such neural substrates exist, then this supports the thesis that the striatum might be segregated in a domain-specific manner. The other issue that this study is aimed at resolving are the contributions of the basal ganglia to the central executive system of working memory or working memory in general. This aspect of working memory is used in the widest range of cognitive performance and has been linked to reliable differences in reasoning abilities. The set of fMRI experiments proposed under Specific Aim 2 are aimed at identifying areas within the basal ganglia that are involved in central executive processes. The proposed study aims to identify discrete components involved in working memory within the basal ganglia that can be utilized to identify specific functional loss due to neuroanatomical lesions that occurs in clinical populations, such as in patients with Huntington's disease, Parkinson's disease, Schizophrenia, and Tourette's syndrome.

1F31MH012303-01
PRATT, WAYNE
SPACE AND REWARD INTEGRATION IN THE NUCLEUS ACCUMBENS
UNIVERSITY OF UTAH
SALT LAKE CITY, UTAH

DESCRIPTION (Adapted from applicant's abstract): The present proposal seeks to examine the contributions of afferent inputs to the representations of reward and space that are found within the nucleus accumbens (NAS). Specifically, it is hypothesized that a primary output region of the hippocampus (the ventral

subiculum) provides the NAS with spatial information, and that the basolateral nuclei of the amygdala (BLA) and medial regions of the prefrontal cortex (mPFC) relay reward-related information. To test this, mNAS neurons will be recorded while rats run a spatial memory task on an eight arm radial maze that contains differential amounts of reward (high or low). Once reward or location-specific neurons are located, inactivations of the subiculum, the BLA and/or the mPFC will occur. It is predicted that inactivation of the subiculum will alter spatial representations within the NAS and disrupt spatial memory. Lesions of the mPFC or BLA are expected to result in attenuation of neuronal responses to reward, as well as decrease the rat's preference for high reward arms. Combined inactivations of the subiculum with either the BLA or mPFC is expected to result in disruptions of both spatial and reward-related correlates. Additional manipulations are proposed to examine changes in NAS representations when cues are rotated, when high and low reward arms are reversed, and when rats are presented with a novel reward. This study seeks to provide initial data on how multiple forms of information are integrated within the medial NAS, which will open the possibility of studying this region's involvement in psychopathology (i.e. schizophrenia).

5F32MH011579-03
PRICE, KIMBERLY
STRESS, PRENATAL VACCINATION AND INFANT IMMUNITY
UNIVERSITY OF WISCONSIN
MADISON, WISCONSIN

Stressors during prenatal development may be particularly potent in contributing to an individual's disease vulnerability later in life by affecting the rate of maturation and the establishment of certain immune responses. The goal of this research is to further examine the immunological consequences of gestational experience by evaluating maternal and infant antibody responses to prenatal vaccination under two different prenatal conditions. We propose to measure the passive and active immune responses to prenatal vaccination against Haemophilus influenzae type b (Hib) in pregnant female rhesus monkeys and their infants (Year 1). Once these baseline values are established, females will be subjected to either a psychological stressor paradigm (Year 2) or given moderate levels of alcohol (Year 3) during gestation to test how these factors influence the active immune response to the vaccine in the mother, the placental transfer of anti-Hib antibody to her fetus, and the ability of the infants to mount an active immune response when presented with the vaccine postnatally. We hypothesize that mothers exposed to both disturbance conditions will have a decreased antibody response to the vaccine. Furthermore, while the active placental transfer of antibody may partially compensate for the reductions in maternal antibody, infants born from disturbed pregnancies may have lower antibody levels than those of control infants. Exposure to psychological stress or alcohol prenatally will impair the infant's ability to produce an active antibody response to the vaccine when administered postnatally. Finally, this research will develop the vaccine paradigm as a unique means of assessing the psychobiological well-being of the young infant.

1F31MH012115-01
PRICE, MICHELLE
CORTICOTROPIN-RELEASING FACTOR AND SEROTONIN INTERACTION
UNIVERSITY OF PENNSYLVANIA
PHILADELPHIA, PENNSYLVANIA

DESCRIPTION: The dorsal and median raphe nuclei, the source nuclei of forebrain serotonergic innervation, contain corticotropin releasing factor (CRF) receptor mRNA and are densely innervated with CRF-immunoreactive fibers. Taken with recent findings that demonstrate biphasic effects of CRF on striatal serotonin (5-HT) release and inhibitory effects of CRF on neuronal activity of putative 5-HT neurons in the dorsal raphe nucleus, it is possible that CRF, or a related family member, regulates the activity of the 5-HT system. The objective of this proposal is to examine the physiological interactions between the brain CRF system and the raphe nuclei serotonergic system. Since CRF and 5-HT have been independently implicated in stress and stress-related psychiatric disorders, such as depression and anxiety, we hypothesize that interactions between CRF and 5-HT may be important in mediating the effects of particular stressors. This hypothesis will be tested by the following specific aims: 1) Determine the local mechanism of CRF control of 5-HT release. Pharmacological analysis using CRF receptor agonists and antagonists will be performed. These studies will be used to determine whether CRF-5-HT interactions occur at the level of 5-HT cell bodies. 2) Determine whether CRF effects on forebrain 5-HT release are regionally specific. Dose-response curves for the effects of CRF, administered intracerebroventricularly on 5-HT release in lateral septum, amygdala, nucleus accumbens, and hypothalamus will be generated. 3) Determine physiological conditions during which endogenous CRF affects the forebrain 5-HT system. The ability of a CRF receptor antagonist to block alterations in 5-HT release in terminal regions during physiological stressors will be determined. This aim will provide functional significance for CRF-5-HT interactions and reveal situations in which endogenous CRF interacts with the forebrain 5-HT system.

5F32MH011770-02
PRINSTEIN, MITCHELL
SOCIAL FUNCTIONING AND SUICIDALITY ACROSS DEVELOPMENT
RHODE ISLAND HOSPITAL
PROVIDENCE, RHODE ISLAND

DESCRIPTION (Adapted from applicant's abstract): This investigation will utilize a cross-sectional design to examine the social functioning of a diagnostically heterogeneous group of preadolescents and adolescents hospitalized for suicidal behavior. Social functioning (i.e., friendships and peer relations) has been surprisingly unstudied within the suicide literature, although an examination of suicidal teens' social functioning appears to be a critical area of investigation. For instance, information on the social functioning of suicidal teens would offer some obvious directions for peer-based intervention efforts in this population. Studying suicidal teens' social functioning would also make a substantial contribution to the peer relations literature. Although many studies have investigated peer relations variables in a clinical sample. This study would expand our knowledge in both areas. Participants will include approximately 200 preadolescents (ages 10-12) and adolescents (ages 13-17) who have engaged in suicidal behavior (i.e., suicidal threat, gesture, or attempt) that requires inpatient psychiatric care. As part of an existing research protocol, measures on children's peer group affiliation, friendship quality, diagnostic interview, subjects will be divided into diagnostic groupings: Internalizing Only (e.g., Major Depression, Dysthymia) and a comorbid Internalizing/Externalizing (e.g., Conduct Disorder, Oppositional Defiant Disorder) group. Analyses will address two main study goals. First, differences in social functioning based on age and diagnosis will be examined. Second, the relationship between social

functioning and suicidal behavior will be investigated, as well as the potential moderating effects of age and diagnosis in this relationship.

5F31MH011943-02
PRYBYLOWSKI, KATE
TYROSINE PHOSPHORYLATION AND NMDA RECEPTOR FUNCTION
GEORGETOWN UNIVERSITY
WASHINGTON, D.C.

DESCRIPTION (Adapted from applicant's abstract): The general rationale for thesis project is to study the role of tyrosine phosphorylation in the control of NMDA receptor function. This project will study the specific role of the NR2D subunit as a possible site of modulation. The aims of this project are: (1) to examine mechanisms responsible for changes in NMDA receptor function following increase tyrosine phosphorylation of cells transfected with NR2D and NR1 subunit cDNAs; (2) to determine the sites of tyrosine phosphorylation of the NR2D subunit to verify that tyrosine phosphorylation at this site is responsible for observed functional changes; and (3) to determine that the pattern of increased tyrosine phosphorylation observed in transfected cells is also seen in neurons. This project could give important insights into mechanisms of modulation of the NMDA receptor, which is critical in the effects of the drugs of abuse, phencyclidine (PCP).

1F31MH012148-01
PUGH, C
SELECTIVE CYTOKINE EFFECTS ON LEARNING/MEMORY PROCESSES
UNIVERSITY OF COLORADO
BOULDER, COLORADO

DESCRIPTION (Applicant's Abstract): The proposed research will explore interactions between the immune system and learning/memory processes by testing the hypothesis that pro-inflammatory cytokines selectively influence memory processes mediating hippocampally dependent contextual fear conditions. To determine if pro-inflammatory cytokines are involved in producing the impairment caused by peripheral LPS administration: (1) LPS will be injected while macrophages are inhibited by gadolinium chloride to determine if macrophage activation is necessary to observe the impairment in contextual fear caused by LPS; (2) LPS will be injected concurrently with either a peripheral IL-1beta receptor antagonist, TNF binding protein, or IL-6 antibody to determine if these cytokines are involved in producing the impairment in contextual fear; and (3) zymosan, another immune activator that induces the release of pro-inflammatory cytokines, will be injected to determine if it also impairs contextual but not auditory-cue fear. To determine if central IL-1beta activity is necessary to observe the impairment in contextual fear caused by LPS: (1) LPS will be injected concurrently with a central intracerebroventricular (i.c.v.) IL-1beta receptor antagonist; and (2) LPS will be injected concurrently with hippocampal microinjeted IL-1beta receptor antagonist. To determine if other variables, such as social isolation, that selectively impair contextual fear do so through inducing an increase in hippocampal IL-1beta: (1) it will be determined whether social isolation increases IL-1beta mRNA, and (2) rats will be conditioned and isolated in the presence of hippocampally administered IL-1beta receptor antagonist.

5F32MH011768-02
QUELLER, SARAH
CONNECTIONIST MODELS AND PERCEPTIONS OF ATYPICAL GROUP M

PURDUE UNIVERSITY
WEST LAFAYETTE, INDIANA

DESCRIPTION (Applicant's Abstract): We frequently encounter members of stereotyped groups that do not fit the stereotype, and one might think that these encounters would eventually bring about stereotype change. Intuitively, this should be particularly true when the atypical group members all contradict the stereotype in the same way. However, research indicates that stereotypes are very difficult to change and, in particular, that subgroups of highly atypical group members are subtyped, or mentally segregated from the rest of the group such that they are ineffective in bringing about stereotype change. The studies in this proposal investigate variables that might moderate the effectiveness of highly atypical group members in encouraging stereotype change. In addition, the studies reported here investigate the abilities of connectionist networks to modeling learning about atypical group members. Connectionist models of memory are receiving substantial attention in the cognitive literature, and it is probable that incorporating them into our thinking about social aspects of behavior and thought will serve to 1)encourage thinking about social memory from a new perspective that will potentially lead to new predictions about social phenomena, and 2) allow social phenomena to inform the development of these models that are becoming increasingly prevalent throughout psychology.

5F31MH011753-02
QUIRK, JENNIFER
CALCIUM ACTIVATED K CHANNEL ASSOCIATION DOMAINS
DUKE UNIVERSITY
DURHAM, NORTH CAROLINA

DESCRIPTION (Adapted from applicant's abstract): The focus of this proposal is to identify and characterize protein domains necessary for the assembly of large-conductance KCa) channels. The minimal functional KCa channel is ahomotetramer. Individual subunits must incorporate into the membrane and fold properly, and these subunits then specifically identify, and associate with, like subunits. While KCa channel assembly has not been studied, the assembly of other membrane protein complexes has been examined in some detail, and this knowledge will be used as a guide for the experiments outlined in this proposal. To begin to understand KCa subunit association, the domain(s)necessary for this association will be identified, both functionally and biochemically. Once domain(s) are identified, the question of how association occurs will be addressed by structure-function experiments on the association domain(s). For example, putative electrostatic interactions will be disrupted, and then the effect on association at the functional and biochemical levels will be examined. The identification and characterization of the association domain(s) of KCa channels will provide general information on ion channel assembly, as well as specific information on KCa currents in the CNS.

5F32MH011741-02
RAGOZZINO, MICHAEL
MNEMONIC PROPERTIES OF THE PREFRONTAL CORTEX
UNIVERSITY OF UTAH
SALT LAKE CITY, UTAH

DESCRIPTION (Adapted from applicant's abstract): There is accumulating evidence that the prefrontal cortex is involved in working memory in several mammalian species. Prefrontal cortex damage leads to a variety of working

memory deficits in humans, as well as rodents. These results suggest that the prefrontal cortex may be involved in working memory for different attributes, i.e., space, affect, motor responses. Recent evidence suggests that the type of working memory deficit that results following prefrontal cortex damage maybe related to the lesion site. Understanding whether specific prefrontal cortex subregions mediate different types of information within a working memory context, will lead to important insight into the biology of memory. To build a more comprehensive view of the neural processes that underlie memory within prefrontal cortex subregions, also calls for an examination of the neurotransmitter systems that may play a critical role. The present proposal examines the neural processes in the prefrontal cortex important for working memory of different attributes. The first set of experiments investigates whether there are dissociations between the anterior cingulate, prelimbic/infralimbic and agranular insular in mediating working memory for spatial locations, visual objects, affect and motor responses. Based on previous studies and preliminary data, it is predicted that the anteriorcingulate mediates working memory for motor responses, the prelimbic/infralimbic mediates working memory for space and objects and the agranular insular mediates working memory for affect. The second set of experiments assess whether acetylcholine within prefrontal cortex subregions memory for different attributes. The hypothesis is that the cholinergic system is important in all prefrontal subregions for processing working memory for specific attributes. Overall, these experiments will provide a better understanding of the mnemonic functions mediated by prefrontal cortex subregions and the neurochemical modulation of these functions. Thus, the studies may increase the knowledge about the neurobiology of memory and may ultimately lead to effective treatments for cognitive dysfunctions.

1F31MH012086-01
RALPH, REBECCA
DOPAMINE MODULATION OF PPI AND LMA IN KNOCKOUT MICE
UNIVERSITY OF CALIFORNIA
SAN DIEGO, CALIFORNIA

DESCRIPTION (adapted from the applicant's abstract): Schizophrenia is one of the most prevalent neuropsychiatric disorders in our country today. By establishing the neural substrates mediating specific deficits of this disorder the development of better treatments might be accomplished. PPI (a measure of sensorimotor gating) is a normal cross-species occurrence that is deficient in schizophrenic patients. This impairment in PPI has been successfully modelled in rats through the use of DA agonists and these deficits have been then reversed using DA antagonists and antipsychotics. The goal of this project is to use recently developed "knockout" mice to investigate the role of DA in the modulation of PPI. Background pharmacology studies will be conducted, as few experiments have been done using mice. The second aim of this proposal is to characterize the D2 receptor knockout and the DAT knockout mice in PPI and locomotor activity sessions and investigate pharmacological manipulations of their behavior. In summary, this proposal seeks to determine the role of DA in the modulation of PPI and locomotor activity through the use of genetically altered mice.

5F32MH011252-02
RAMUS, SETH
HIPPOCAMPAL DEPENDENT CORTICAL MEMORY REPRESENTATION
BOSTON UNIVERSITY
BOSTON, MASSACHUSETTS

DESCRIPTION (Adapted from applicant's abstract): The goal of this proposed project is to demonstrate evidence for the time-limited, hippocampal-dependent consolidation of a cortical memory representation. Current theory suggests that the storage of long-term, declarative memories is dependent on interactions between the hippocampal system and neocortex. With the passage of time, memory representations become less dependent on the hippocampal system, until they become permanently consolidated in neocortex. This project will address this goal using electrophysiological and behavioral assessment in an 8-odor serial discrimination task with predictive relationships between odors. The specific aims are: (1) To analyze the development of changes in the firing patterns in the orbitofrontal cortex (OF) associated with learning of predictive relationships between odors (i.e., learning stimulus-stimulus pairing in which the first of two stimuli predicts the ensuing occurrence of the second), both at the level of the neural ensemble. (2) To demonstrate that the behavioral and electrophysiological correlates associated with learning of predictive relationships are dependent on the hippocampal system. (3) To study the time course of the consolidation of these same cortical representations as they gradually become independent of the hippocampal system. This hypothesis will be tested by giving rats ibotenate lesions of the hippocampal region at varying times after learning the predictive relationships between odors, and by reversibly inactivating the hippocampal region with muscimol at varying times during performance of the memory task.

5F32MH011150-03
REBER, PAUL
NEUROPSYCHOLOGICAL STUDIES OF IMPLICIT MEMORY
UNIVERSITY OF CALIFORNIA
SAN DIEGO, CALIFORNIA
DESCRIPTION (Adapted from applicant's abstract): One important source of data leading to notion of functionally distinct memory systems is the finding that amnesic patients, who are impaired on a wide range of memory tasks, can never-the less exhibit normal learning on many tasks presumably supported by nondeclarative (implicit) memory. Recent work I have just completed with amnesic patients further indicates that declarative and nondeclarative memory have different operating characteristics. Declarative memory affords awareness and supports the flexible use of task knowledge in situations different from the original learning while nondeclarative memory does not afford awareness and is relatively inflexible. Three experiments are proposed here that continue to investigate dissociable properties of declarative and nondeclarative memory. The first addresses the debate as to whether implicit memory stores only fragmentary specific knowledge from the learning experience or whether implicit memory is also capable of storing abstract rules. The second experiment further examines of nondeclarative memory. The third experiment investigates the role of implicit memory in problem solving by asking whether amnesic patient sex hibit a bias in problem solving towards previously successful strategies. Together these experiments will enhance our understanding of the operation of implicit memory and its role in high-level cognitive function.

5F31MH011659-03
REPA, J
PLASTICITY IN SENSORY INPUT PATHWAYS TO THE AMYGDALA
NEW YORK UNIVERSITY
NEW YORK, NEW YORK

DESCRIPTION (Adapted from applicant's abstract): Several psychiatric disorders, including phobias, panic, posttraumatic stress disorder, and anxiety, are based in part on fear-related emotional memories. Understanding the neural plasticity which underlies emotional memories is critical to the development of treatments for such disorders. The study of the neural substrates of plasticity have been much advanced by the use of a classical fear conditioning paradigm, during which an aversive association is formed with a previously innocuous conditioned stimulus (CS) after pairing the CS with an aversive unconditioned stimulus (US). A large body of evidence points to the amygdala as an integral structure in the neural system that mediates fear conditioning; furthermore, lesion studies have shown that when the CS is an auditory stimulus, fear conditioning can be induced through either a direct thalamo-amygdala or an indirect thalamo-cortico-amygdala pathway. The proposed research develops a preparation which permits a characterization of conditioning-induced plasticity along these sensory input pathways to the amygdala at the level of individual neurons, in awake behaving rats. Multiple single neurons will be simultaneously recorded from, throughout fear conditioning, in the lateral nucleus of the amygdala (LA) and two regions that send monosynaptic efferents to the amygdala, in the auditory thalamus and cortex. In addition, synaptic efficacy of each of these two pathways will be measured before and after fear conditioning through single unit and evoked potential responses in LA to electrical test stimulation of these two pathways. Finally, lesioning one pathway at a time, prior to fear conditioning, will inform us about the contribution of each pathway to the acquisition of neural plasticity.

5F31MH011907-02
REYES, TERESA
CYTOKINE CASCADE--A PATHWAY TO THE BRAIN
UNIVERSITY OF WISCONSIN
MADISON, WISCONSIN

DESCRIPTION (Adapted from the Applicant's Abstract): This application seeks to explore avenues by which the periphery communicates with the brain, and the consequences of this communication for mediating immune responses. This application intends to study the elaboration and effects of interleukin 6 (IL-6) following peripheral administration of IL-1. Three studies are to be undertaken as part of this predoctoral application. These studies attempt to(1) identify a possible cellular source of IL-6 in cerebrospinal fluid (CSF), namely, endothelial cells, (2) analyze IL-6 bioactivity in blood and intrathecal compartments, (3) define potential functions of IL-6 in the CSF. Monkey endothelial cell cultures will be established to examine whether these cells can produce IL-6 upon stimulation with IL-1. To attempt to localize the source of IL-6, blood and different intrathecal compartments will be sampled after peripheral injection of IL-1 to determine if different concentrations of IL-6 can be found in these compartments. Finally, bioactivity of blood and influence of CSF (both with and without IL-6) on lymphocyte proliferation will be investigated to assess effects of IL-6 on an immune response of interests. These findings are suggested to be relevant to diseases with neuroimmunesequelae, involving high cytokine levels of leukocyte infiltration into the CNS.

5F31MH011369-03
RHEN, TURK
EVOLUTION AND BEHAVIORAL ORGANIZATION
UNIVERSITY OF TEXAS
AUSTIN, TEXAS

DESCRIPTION (Adapted from applicant's abstract): Rodents and primates have been used as models for human behavior. Studies in these species are limited in their ability to determine why sexual and aggressive behaviors are organized to a greater degree in male mammals. Two alternate explanations of this pattern are that 1) the sex determining mechanism (XY males) causes organization or 2) that organization is evolutionarily adaptive. These hypotheses make different predictions for organization in different vertebrates. These alternate predictions will be tested in gonadectomized male and female lizards from two egg incubation temperatures. Geckos will be implanted with Silastic tubing containing cholesterol, dihydrotestosterone, testosterone, or estradiol. Patterns of male- and female-typical behavior exhibited by these groups when treated with sex steroids will distinguish among the following hypotheses: 1) there is no organization, 2) organization is caused by incubation temperature, 3) one sex is organized by incubation temperature and the other sex is unorganized, 4) one sex is organized as in mammals (or birds), or 5) both sexes are organized. Also hypothesized, 1)there are steroid-induced changes in molecular neuroendocrinology as measured by in situ hybridization of mRNA and 2) changes are correlated with behavioral organization. Hormone treatments that activate male-typical behavior may affect androgen receptor (AR) mRNA, estrogen receptor (ER) mRNA, progesterone(PR) and/or aromatase mRNA levels in the preoptic area of the brain. Hormone treatments that activate female-typical behavior may affect AR, ER, and PRm RNA levels and possibly aromatase mRNA in the ventromedial hypothalamus. Hormone treatments that activate aggression may affect AR, ER, PR, and/or aromatase mRNA levels in the amygdala. The bases of sexual and aggressive behavior in this species may provide insight into mechanisms of "abnormal" behavior in humans. For example, aberrant organization (via genetic and/or environmental causes) in humans could result in "abnormal" behavior.

5F32MH011550-02
ROGERS, RONALD
NEURAL CORRELATES OF CONTEXTUAL-BASED LEARNING
INDIANA UNIVERSITY
BLOOMINGTON, INDIANA

DESCRIPTION (Adapted from applicant's abstract): A research project is proposed that will build on the recent demonstration of contextually-based conditional discrimination during rabbit eyelid conditioning. Specifically, this project will investigate the participation of deep cerebellar nuclei and the hippocampal formation in this form of learning. Three experiments will: 1) map single unit activity in the interpositus nucleus during conditional discrimination, 2) chemically lesion the dorsal hippocampus both prior to and after learning of the discrimination, and 3) record single unit activity from CA1 throughout discrimination learning. These endeavors should result in amore complete understanding of the contribution of these brain areas to contextual learning and its ability to modulate associative responding. Additionally, this work should provide a greater understanding of limbic-cerebellar interactions during simple motor learning.

5F32MH011112-03
ROSENTHAL, SAUL
SOCIAL RESPONSIBILITY AND THE DEVELOPMENT OF COMPETENCE
UNIV OF MED/DENT NJ-R W JOHNSON MED SCH
PISCATAWAY, NEW JERSEY

DESCRIPTION (Adapted from applicant's abstract): While we believe a healthy society is one in which members contribute to the general well-being, there is little research or theory regarding the development of citizenship. The purpose of this project is to provide data that characterizes citizenship and behaviors in adolescence and young adulthood, and identifies antecedent child, family, and environmental factors that contribute to the expression of citizenship. Existing research on prosocial development tends to be retrospective and focused on laboratory-based or simple situations. This project involves a long-term prospective study that is designed to better our understanding of naturally occurring prosocial behavior and the factors that relate to such behavior. Subjects have participated in a longitudinal study of social, cognitive, and behavioral development from infancy through 18 years. At 18 years, data were collected on subjects' volunteer activities, prosocial reasoning, and their altruistic attitudes, which were hypothesized to represent multiple facts of citizenship. Further, it is hypothesized that antecedent factors will differentially predict aspects of citizenship. Work to date has shown that citizenship is not necessarily a unitary concept. This suggests that there may be different developmental pathways for volunteering, altruism, and reasoning, which this proposal is designed to study. The first of two studies described in this proposal is designed to examine the development of citizenship, determining the effects of individual family, and environmental factors on volunteering, altruism, and reasoning. In addition to examining citizenship at a particular time, it is necessary to determine how citizenship changes. In the second study described in this proposal, citizenship information will be collected from subjects when they are young adults. This way, we can determine whether individuals change their attitudes and behaviors as they transition into adulthood. Furthermore, we will be able to determine whether antecedent events are related to those changes. The following are the specific goals of this proposal: 1) to determine antecedent individual, family, and environmental factors of citizenship at 18 and 21 years of age; and 2) to determine the ways citizenship changes from adolescence through adulthood.

1F31MH011982-01A1
ROTH, JONATHAN
DUAL ANORECTIC TREATMENT IN RATS--EFFICACY AND SAFETY
UNIVERSITY OF FLORIDA
GAINESVILLE, FLORIDA

DESCRIPTION (Adapted from applicant's abstract):
The recent withdrawal of dexfenfluramine (DFEN) from the market has left many obese individuals and their clinicians without effective pharmacological tools. Behavioral programs (e.g., diet, exercise) alone have notoriously poor records of long-term success in combating obesity. The most popular and apparently effective drug regimen prior to the withdrawal was phentermine (PHEN) and DFEN. It is important to understand why the DFEN/PHEN combination was so effective, and to use this information to drive drug discovery programs and treatment regimens. Astonishingly, there is little available animal literature on the behavioral efficacy of DFEN/PHEN, data that would form the foundation of assessing combination effects. Three main studies are proposed in this revised application. First, an isobolographic analysis of whether DFEN/PHEN's anorectic effects are simply dose-additive of each drug or are supra-additive (implying a synergistic mechanism). The second study is a pharmacological study of the mechanisms of the combination using selective adrenergic and serotonergic antagonists. The third proposed study will investigate the sites of action of the

combination in the brain using Fos immunoreactivity as an index of neural activation. Potentially, these results will provide useful information toward the future development of more effective anorectics. On a broader level, examining the combined effects of anorectics that target different transmitter systems represents a useful model for evaluating how neurotransmitters interact to control feeding behavior.

5F32MH012002-02
ROUSE, SUSAN
MUSCARINIC ACTYLCHOLINE RECEPTORS IN PERFORANT PATHWAY
EMORY UNIVERSITY
ATLANTA, GEORGIA

DESCRIPTION (Adapted from applicant's abstract): In the brain, acetylcholine(ACh) has been demonstrated to be involved in many higher cognitive functions including learning and memory. Specifically, the involvement of muscariniccholinergic transmission in learning and memory has been demonstrated in the hippocampus and neocortex. Neurological disorders, such as Alzheimer's Disease, that involve a deficit in memory function are characterized by a loss of cholinergic innervation of the cortex and hippocampus from the basal forebrain. Recently, 5 muscarinic receptor subtypes (m1-m5) have been identified by molecular cloning techniques and four of those subtypes (m1-m4)have been localized to the hippocampus utilizing subtype specific antibodies. Several diverse modulatory functional have been attributed to muscar inicreceptors in the hippocampus, including the reduction of synaptic transmission at the perforant path/granule cell synapse by muscarinic agonists. Until recently, the assignment of such functions to individual receptor subtypes has been hindered by the lack of specific pharmacological tools to discriminate between subtypes. However, detailed localization studies have implicated individual receptor subtypes in the cholinergic depression of perforant path transmission. Moreover, recently developed subtype-specific agonists and antagonists now allow for the physiological matching of mAChR subtypes and their specific functions. The following proposed research will use electrophysiological approaches to define the mechanism and receptor subtype responsible for cholinergic modulation of the perforant path/granule cellsynapse as a first step in understanding how individual mAChR subtypesmodulate hippocampal functioning.

1F31MH011925-01A1
SAEZ, EMILY
FAMILY ENVIRONMENT AND DEPRESSION IN ADOLESCENTS
UNIVERSITY OF PUERTO RICO RIO PIEDRAS
RIO PIEDRAS, PUERTO RICO

DESCRIPTION (Adapted from applicant's abstract):
This is the first revision of an individual research fellowship application. The principal objectives of the proposed research are to evaluate the relationship among family functioning, parental depression, parental marital conflicts with depression, and to evaluate the relationship between marital conflicts and behavior problems in Puerto Rican adolescents. Adolescent depression is one of the most common psychological disorders manifested in this population. Although the number of investigations in depression have increased in the last decades, the need to carry out studies in this area is essential, specifically in Hispanic populations. It is important to identify the particular characteristics associated to depressive symptomatology in Hispanics in order to develop effective preventive interventions and

treatment for this population. Taking into consideration that family environment is very important to Hispanics, the specific aims of the research proposal are to evaluate: 1) the relationship between family functioning and depressive symptomatology in adolescents; 2) the relationship between perceived marital conflicts and depressive symptomatology; 3) the relationship between perceived marital conflicts and behavioral problems; 4) the relationship between marital satisfaction and depressive symptomatology in parents; 5) the relationship between parental depressive symptomatology and depressive symptomatology in adolescents. In addition, in this study gender, age, residential zone differences will be evaluated. The predictive values of these variables on depression will be explored. All of these relationships will be evaluated in a community and in a clinical sample, and also a comparison between the two samples will be carry out. The sample of this research will consist of two community and clinical sub-samples. The community sample will be selected from students (and their parents) of a public intermediate school and a public high school of a city in the center area of Puerto Rico. Participants of the Adolescents Depression Project, directed by Dr. Rossello will constitute the clinical sample of this investigation. These participants are adolescents who present depressive symptomatology and are going to take individual or group psychotherapy as treatment for depression. After the sample is selected, several instruments will be administered to the adolescents and their parents. The instruments that will be administered to adolescents are: 1) Children's Depression Inventory, 2) Child Behavior Checklist, 3) Family Assessment Measure, 4) Family Emotional Involvement and Criticism Scale, and 5) Children's Perception Questionnaire. The following instruments will be administered to the parents: 1) Beck Depression Inventory and 2) Dyadic Adjustment Scale. To analyze the information obtained from the self-report instruments administered to adolescents and their parents, differents statistical analyses will be carry out (correlational analysis, multiple regression analysis, analysis of T-test to evaluate differences between variables and between correlations).

1F31MH012247-01
SAGE, JENNIFER
MNEMONIC FUNCTIONS OF THE BASAL GANGLIA
UNIVERSITY OF CALIFORNIA
LOS ANGELES, CALIFORNIA

DESCRIPTION (Adapted from applicant's abstract): The primary objective of this project is to use an interdisciplinary approach to study implicit memory functions of the basal ganglia, with a focus on habit learning. Habit learning refers to the gradual, incremental acquisition of performance-based associations. Both humans with basal ganglia dysfunction (e.g., Parkinson's and Huntington's disease) and rats with caudate nucleus lesions show impairments on habit learning tasks. Studies using both rat and human models of neostriatal learning and memory are included in this proposal, in order to provide a more integrative framework in which to study this system. Since previous studies have demonstrated dissociable memory deficits with basal ganglia and hippocampal dysfunction, it is important to understand the characteristics of learning that each system mediates. The caudate-dependent win-stay radial maze task will be used to examine the nature of associations learned by the basal ganglia in rats. These findings will be contrasted with the nature of associations learned by the hippocampus, on a hippocampal-dependent win-shift maze task. In addition to this behavioral characterization, it is important to map out the critical components of the habit learning system. The neural basis of habit learning will be explored by examining effects of exciotoxic lesions of the basal

ganglia and related structures, on win-stay maze learning. In addition, a rat model of Parkinson's disease and its anticipated reversal by pallidotomy will be assessed on this task. In human Parkinson patients, the effect of pallidotomy on habit learning deficits associated with the disease will be explored. Although these patients often show greatly improved motor symptoms, the effects of this brain lesion on cognitive processes have not been fully examined.

5F31MH011735-02
SAILSTAD, CYNTHIA
NEURAL MECHANISMS CONTROLLING RECEPTIVE FIELD PARAMETERS
MOUNT SINAI SCHOOL OF MEDICINE OF CUNY
NEW YORK, NEW YORK

DESCRIPTION (Adapted from applicant's abstract): Several theories concerning the nature of visual processing and architectural function of the primary visual cortex have evolved from the basic understanding of the receptive field characteristics and how these receptive fields interact at different cortical levels. Current evidence indicates that in the adult primate and cat cortex, receptive field properties show a significant degree of integration occurring in the primary visual area (V1). The degree of receptive field modifiability and its neurological substrate, however, remain controversial. (Pettet &Gilbert, 1992, DeAngelis et. al. 1995). The goal of this project is to determine the role of the long range lateral connections in generating receptive field malleability after exposure to an artificial scotoma. The study will investigate three possible synaptic mechanisms by which intrinsichorizontal connections could modify the RF properties. Their effect may be due to an increase in synaptic efficacy, due to a general increase inexcitability, or due to specific inhibitory and/or excitatory postsynaptic input. The experimental approach of this study incorporates the artificial scotoma electrophysical techniques established by Pettet & Gilbert (1992), and DeAngelis et. al (1995). However, this proposal expands upon their methodology in two different ways: 1) pharmacological manipulations will be used to explore the possible synaptic mechanisms; and, 2) tetrodes will give amore complete picture of the scotoma's effects on the population of cortical neurons. These two modifications will help to obtain greater insight into the degree of RF malleability and the possible mechanisms generating these changes. Ultimately, this information will help to give a deeper understanding of how the primary visual cortex integrates information to form visual perception and imagery.

1F31MH011855-01A1
SALAT, DAVID
FRONTAL LOBE ATROPHY IN ALZHEIMERS DISEASE AND AGING
OREGON HEALTH SCIENCES UNIVERSITY
PORTLAND, OREGON

DESCRIPTION (Adapted from applicant's abstract):
The overall goal of the proposed studies is to examine the role of frontal lobe atrophy in the behavioral and cognitive changes of healthy aging and Alzheimer's disease. The aims of the studies proposed are: 1) to examine whether frontal lobe atrophy is similar or has a distinct pattern in Alzheimer's disease as compared to healthy aging; 2) to determine if frontal lobe atrophy in specific regions of interest (ROI) of the frontal lobe predicts which cognitively intact healthy elderly will subsequently develop Alzheimer's disease; and 3) to determine the relationship between cognitive and social behavioral abilities and frontal lobe volume in healthy elderly and patients with Alzheimer's

disease. These studies will be accomplished by calculating and comparing volumetric data on five ROIs from MR scans of healthy aged, Alzheimer's disease patients, and subjects with incipient dementia. Cognitive and behavioral data collected for Aim 3 will be related to ROI volumes to determine the consequences of frontal lobe atrophy on cognitive functioning in healthy aging and Alzheimer's disease.

5F32MH011706-02
SALO, RUTH
FRONTAL LOBE AND SEQUENTIAL PROCESSES IN SCHIZOPHRENIA
UNIVERSITY OF CALIFORNIA
DAVIS, CALIFORNIA

Both patients with schizophrenia and patients with frontal lobe lesions have been described as deficient in suppressing irrelevant information. Recent findings, suggest that both patient groups may be capable of inhibiting distracting information when the stimuli are immediate, but exhibit impairments in sustaining inhibition over time. The sustainment of information across time require not only the maintenance of a memory trace, but the suppression of competing stimuli. As many parallels have been suggested in the literature between frontal lobe pathology and schizophrenia, it is critical to understand the links between symptomatology and cognitive behavior within these patient groups. This project proposes to investigate the temporal parameters of selective inhibitory processes in both patients with schizophrenia and patients with lesions to the prefrontal cortex. By the use of rigorous patient diagnostic screening, symptom assessment, clinical neuropsychological tests and computerized reaction time measures of inhibitory processes, the time course of inhibition in these two patient groups can be analyzed. Several experiments (see section 29.B) investigate: 1) the sustainment of inhibition at several inter-trial intervals; 2) the correlation between sequential inhibitory processes and clinical symptomatology; and 3) the sequential processing of relevant and irrelevant information. The comparison of the patterns of inhibitory deficits in neurological patients and patients with schizophrenia will elucidate the contribution of the prefrontal cortex in maintaining inhibition across time.

1F31MH012069-01
SAMUELSON, LARISSA
EARLY WORD LEARNING--COMPUTATIONAL AND BEHAVIORAL TESTS
INDIANA UNIVERSITY
BLOOMINGTON, INDIANA

DESCRIPTION (Applicant's Abstract): Children are amazing word learners. Even though the number of possible meanings for each novel word is immense, children learn words quickly and with seemingly little effort. Previous research has suggested that children are biased to only consider some of the possible meanings for a new word. However, the origin of word learning biases and the mechanisms by which they operate on a moment-to-moment basis has yet to be determined. The proposed project addresses this gap in our understanding of word learning. In three projects, I will test the hypothesis that word learning biases develop out of statistical regularities in the language and categories children learn. The specific questions addressed are: (1) what are the statistical regularities in the language input of children; (2) can a simple learner of statistical regularities replicate the development of specific word-learning biases; and (3) if the

statistical regularities found in the words children know are altered, does the developmental trajectory of specific word learning biases by change? These questions are addressed in neural network simulations of the development of specific word learning biases; experimental studies in which the natural development of a word learning bias is altered by teaching children words; and in modeling of the changes in word learning that arise from the lexical training.

1F30MH012250-01
SANGORAM, ASHVIN
CIRCADIAN RHYTHMS IN CLOCK KNOCKOUT MICE
NORTHWESTERN UNIVERSITY
SKOKIE, ILLINOIS

DESCRIPTION (applicant's abstract): It is known that Clock is involved in the regulation of circadian rhythms in mice. By positional cloning of an N-Ethyl N-Nitrosourea-induced mutant, a dominant negative allele of Clock was identified. The question of the necessity of Clock for rhythmicity has not bee answered. In per and tim mutants, null alleles of the Drosophila clock genes period and timeless, respectively, locomotor activity rhythms and molecular oscillations in per and tim mRNAs are abrogated. Thus we predict that the Cloc null allele would also result in arrhythmicity in wheel running if it is a bon fide circadian clock component. In addition, the identification of putative period homologues in mice, mPer1 and mPer2, allow us to address the question o whether Clock is essential for molecular oscillations in these putative clock components. Gene targeting affords the opportunity to generate a null Clock allele in vivo to determine the effects on behavioral and molecular oscillations in the mouse. Clock is a member of the bHLH-PAS family of transcriptional regulators. We will create a null allele by replacing the exon encoding the start of translation, the bHLH and part of the PAS domains with the neomycin phosphotransferase gene by homologous recombination in embryonic stem cells. Cell lines will then be used to generate mice homozygous for the null allele (knockout) by chimera aggregation and the appropriate breeding. Knockout mice will be examined for alterations in wheel running activity as a behavioral measure of their circadian rhythms. Knockout mice will also be examined for effects of the loss-of-function allele on the molecular oscillations of mPer1 and mPer2 by in situ hybridization. Our overall objectiv is to learn whether Clock is essential for behavioral and molecular rhythmicit in mice.

5F32MH011704-02
SAVASTANO, HERNAN
CONTEXT AND TIMING ON ASSOCIATIVE LEARNING
STATE UNIVERSITY NEW YORK
BINGHAMTON, NEW YORK

DESCRIPTION (Adapted from applicant's abstract): The general aim of this proposal is to shed light on the distinction between learning and the rules that govern the behavioral expression of that learning. Specifically, the studies are designed to explore the role that contextual and timing variables play in defining the nature of associative learning. Current theories of conditioning differ on whether the effect of context (variables separate from the target contingency) on observed behavior is best construed as variation in learning or expression. One set of studies involves manipulating the training context in various ways and subsequently testing what was learned by employing converging measures, specifically by measuring the eliciting power and reinforcing power of the target stimulus. Whereas learning models claim that

context should influence both associative functions equally, expression model scan be interpreted as predicting a divergence between these indices of learning. Another set of studies examines Ralph Miller's (the sponsor)temporal coding hypothesis, which claims that mere contiguity is sufficient for the formation of an association but insufficient for expression of that learning. A greater understanding of how basic learning processes operate with animals in simple conditioning situations will eventually enable us to better understand how humans learn to associate events in their environment. Such knowledge will likely contribute to the development of treatments of maladaptive behaviors and facilitation of education.

1F32MH011902-01A1
SCHAFE, GLENN
CREB LTP AND FEAR MEMORY
NEW YORK UNIVERSITY
NEW YORK, NEW YORK

DESCRIPTION (Adapted from applicant's abstract): This proposal is aimed at defining the molecular mechanisms that underlie the consolidation of classically conditioned fear in the thalamic pathway between the medial geniculated body (MGB) and lateral amygdala (LA), a site that the neuroanatomical and pharmacological studies have suggested to be critical for the plastic changes underlying fear conditioning. In a series of behavioral and immunohistochemical experiments, we will first assess the role of both protein synthesis and the cAMP-CREB cascade in LA on the acquisition and long-term retention of conditioned fear. Subsequently, we will employ electrophysiological methods to examine the involvement of these processes in the induction and maintenance of long term potentiation (LTP) in LA following tetanic stimulation of the geniculo amygdala pathway. It is hypothesized that interference with protein synthesis or the cAMP-CREB cascade will disrupt both the long-term retention of fear memory and LTP in LA, a result that would be consistent with a large body of evidence implicating this intracellular pathway in the long-term neural and behavioral changes that accompany learning in a wide variety of species and preparations. Further investigation into the neural mechanisms of conditioned fear is expected to shed light on normal processes governing learning and memory in the mammalian brain in general, as well as provide a potential model for the study of the etiology and treatment of psychological disorders in humans, including anxiety, phobic and panic disorders in which fear is a prominent underlying symptom.

5F32MH011609-02
SCHELL, MICHAEL
FUNCTIONAL AND PATHOLOGIC ROLES OF GAP1 IP4BP IN BRAIN
JOHNS HOPKINS UNIVERSITY
BALTIMORE, MARYLAND

The aim of this research is to understand the roles of inositol polyphosphates and their specific binding proteins in controlling the homestasis of calcium in brain. It is known that brief excitotoxic insults to hippocampal pyramidal cells causes their demise, but only days after the insult. This observation raises the possibility that medical treatments might be developed which could be administered after a stroke, seizure, or heart attack to reduce the subsequent delayed neuronal damage. The biochemical events occurring between the insult and the death are not understood, but involve aberrations in calcium homeostasis. The proposed experiments will use fluorescent imaging to examine normal and

pathological calcium dynamics in cultured neuronal and glial cells. To understand the molecular mechanisms underlying the responses, the focus will b GAP1IP4BP, an inositol tetrakisphosphate (IP4) binding protein that interacts with the Ras signalling pathway. This protein lies at a crucial branch point in cellular signalling and may link the changes in intracellular calcium after toxic insuts to the subsequent death of neurons. Initial studies will establish expression levels of GAP1IP4BP and IP4 levels in the cultured cells. Neurons and glia will then be microinjected with blockers and stimulators of the GAP1IP4BP signal transduction pathways, and the spatiotemporal changes in intracellular calcium dynamics will be visualized in individual cells. Once the normal calcium response neurons is characterized, the cells will be exposed to excitotoxic insults and then injected with various molecular probes of the IP4 signal transduction pathways in an attempt to modify the calcium dynamics.

5F32MH011534-03
SCHIML, PATRICIA
NEUROBEHAVIORAL ADAPTATIONS, HORMONES, AND STRESS
UNIVERSITY OF VIRGINIA
CHARLOTTESVILLE, VIRGINIA

DESCRIPTION (Adapted from applicant's abstract): Although high levels of glucocorticoids are commonly linked to stress and impaired reproduction, there are species which show elevations in these steroids during breeding readiness. In musk shrews interactions between males and females are marked by an initial aggressive phase, followed by a rapid transition to receptivity and copulation. Studies will examine interactions between the adrenal glucocorticoids and reproduction in male and female shrews. The primary hypotheses are that adrenal steroids increase during breeding interactions, facilitate display of sexual behavior and modify the neuronal substrates that influence reproductive success. New radio-immunoassays will be developed to measure glucocorticoids over the course of a mating bout. Classic removal and replacement techniques will be used to determine if glucocorticoids facilitate the display of sexual behavior. The distribution of glucocorticoid receptors in the musk shrew brain will be assessed. Double antibody immunocytochemistry will be conducted to locate GnRH containing-cells that may be directly affected by glucocorticoids via glucocorticoid receptors.

1F31MH012015-01
SCHMADER, TANYA
DIFFERENTIATING SELF FROM GROUP--IS IT SELF PROTECTIVE
UNIVERSITY OF CALIFORNIA
SANTA BARBARA, CALIFORNIA

DESCRIPTION (Applicant's abstract): The proposed research is part of a larger attempt to understand the psychological processes by which members of socially devalued groups protect and maintain a positive view of themselves in the face of societal rejection. In particular, this research explores a particular process of self-protection, positive differentiation. For members of socially devalued groups, defining oneself in terms of group attributes can have negative consequences for personal self-esteem. By positively differentiating oneself from other members of one's group, however, the individual is able to avoid these negative consequences and maintain a positive view of him or herself. Although previous findings suggest that members of socially devalued groups do differentiate themselves from fellow group members by rating themselves more positively on a variety

of personal attributes, almost no research has specifically examined cognitive process which mediate positive differentiation and the self-protective function of utilizing this strategy. Two studies are proposed which address these issues. Study 1 utilizes participants' reactions times to test the hypothesis that attributes which positively differentiate individuals from a socially devalued group are more cognitively accessible than those which are equally shared by the individual and the group. Study 2 tests the self-protection hypothesis by varying the availability of positive differentiation as a strategy and measuring resulting changes in self-esteem.

5F32MH011157-03
SCHRAUF, ROBERT
CULTURAL EFFECTS ON RETENTION IN AUTOBIOGRAPHICAL MEMORY
DUKE UNIVERSITY
DURHAM, NORTH CAROLINA

DESCRIPTION (Adapted from applicant's abstract): The research focuses on the effects of culture on cognition, specifically the effects of change of culture(migration) on the distribution of memories across the life span. Subjects are bilingual/bicultural Puerto Ricans who have migrated permanently to angloenviron-ments in the U.S. after growing up on Puerto Rico. Methods of cued recall will be used to test for: (1) a diminished fund of memories for events prior to migration, (2) differential access to memories according to cuing in the mother tongue or second language, and (3) a new concentration of memories("reminiscence bump") corresponding to the development of a new identify as a result of migration. Content analysis of memories recorded by subjects will be used to test for memory vividness and extract cultural and ethnopsychological themes.

1F32MH012169-01
SCHULTZ, LAURA
CALCIUM DYNAMICS IN HIPPOCAMPAL CA1 INTERNEURONS
SALK INSTITUTE FOR BIOLOGICAL STUDIES
SAN DIEGO, CALIFORNIA

DESCRIPTION: This project will utilize a combination of confocal imaging, whole-cell patch recording and anatomical reconstruction techniques to examine interneuronal calcium dynamics in the hippocampal slice preparation. Specifically, it will be aimed at characterizing the spatiotemporal distribution of voltage-gated calcium channels along the somatodendritic axis of various subtypes of CAl interneurons, a topic which is relevant to my long-term goal of studying synaptic plasticity at connections onto interneurons. Should it be the case that active calcium conductances are present on the dendrites of interneurons, my future work would be directed at determining whether interneurons support the same forms of Hebbian plasticity that have been characterized in principal cells. Furthermore, given that there are separate lines of evidence that dysfunctional interneurons and voltage-gated calcium channels contribute to epilepsy, this research could provide additional insight into the nature of epileptogenesis.

5F30MH011239-04
SHARKEY, KATHERINE
PHASE SHIFTING AND SEDATIVE EFFECTS OF MELATONIN
RUSH UNIVERSITY
CHICAGO, ILLINOIS

DESCRIPTION (Adapted from applicant's abstract): This research plan describes two studies that test different properties of the neurohormone melatonin in humans undergoing a large shift in their sleep-wake schedule. The first is afield study to determine whether appropriately-timed melatonin administration can help shift the internal circadian pacemaker to adjust to a 9-hour shift in the sleep-wake schedule. In this protocol, 48 subjects will undergo a 9-hour advance or delay in their sleep-wake schedule for 8 days. Subjects will be randomly assigned to take placebo or melatonin on the first 4 days of the shifted schedule. Phase will be measured using continuous recording of core body temperature. In the second study, the applicant will test melatonin's efficacy in improving sleep during the day after night work without shifting endogenous circadian phase. Subjects (N=10) will each participate in a melatonin trial and a placebo trial. After a week of baseline sleep, subjects will come to the laboratory for 2 nights of simulated night work followed by daytime sleep. Sleep will be polysomographically-recorded on 2 baseline nights, 2 day sleep episodes, and 1 recovery night. In addition, subjects will undergo multiple sleep tests and performance tests during the night work episodes.

5F32MH012004-02
SHERFF, CAROLYN
CELLULAR ANALYSIS OF MEMORY STAGES IN APLYSIA
YALE UNIVERSITY
NEW HAVEN, CONNECTICUT

DESCRIPTION (Adapted from applicant's abstract): This project is part of along-term study of the cellular mechanisms underlying the formation of memory. Memory is known to exist in several temporal stages, including short-term and long-term memory. These stages have temporal counterparts in model systems of synaptic plasticity including serotonin (5HT)-induced synaptic facilitation at sensory neuron-motor neuron synapses in the marine mollusc, Aplysia, where three temporal stages of facilitation have been described: short-term (STF),intermediate-term (ITF) and long-term (LTF) facilitation. These stages can be induced independently at synapses in the pleural-pedal ganglia by applying 5HT only to the presynaptic soma or only to the synapse. This is possible because the presynaptic soma is in the pleural ganglion, while the synapse is in the pedal ganglion. The specific goals of this proposal are to investigate the cellular mechanisms involved in the induction of each stage, the site(s) where these processes occur (presynaptic vs postsynaptic, soma vs synapse), and how processes in different locations can interact to induce long-term changes in synaptic efficacy. Standard microelectrode recording techniques will be used to record from tail sensorimotor synapses in the pleural-pedal ganglia of Aplysia. A plexiglas barrier will be used to separate the bathing solutions of the presynaptic soma from the synapse. Facilitation will be induced with bath application of 5HT. Serotonin and blockers and agonists of second messenger systems and RNA and protein synthesis will be bath applied to either the presynaptic soma or to the synapse or will be injected into single neurons.

5F31MH011806-02
SHERMAN, SUSAN
EXPLORING RISK FACTORS OF HIV AMONG WOMEN
JOHNS HOPKINS UNIVERSITY
BALTIMORE, MARYLAND

DESCRIPTION (Applicant s Abstract):

The primary area of research will be the risk factors which place women at risk of HIV. Women are the fastest growing population developing HIV infection (CDC, 1994). There are a complex array of factors which place certain women at a greater risk of HIV. Some of these risk factors include substance abuse patterns, sexual and physical violence, unsafe sexual practices with high risk partners, multiple sex partners, and broader issues of access to health care and economic disparity As a result of the constellation of these risk factors, inner city African American women are at a disproportionate risk for HIV infection. African American women are approximately 13 times more likely than white women to contract AIDS (Mays, 1989).

Sexual practices and substance use behaviors are the two most widely recognized risk factors for HIV. In 1994, 45% of women with reported cases of AIDS in the United States were current or former intravenous drug users, and 18% were infected as a result of heterosexual contact with male partners who contracted HIV through intravenous drug use (Centers for Disease control and Prevention). Recently, the role of violence has been questioned as a primary risk factor for HIV (Wingood, 1992; Fullilove, 1990). Two of the greatest public health crises in America, HIV and violence, are concentrated in America~s inner-cities and disproportionately affect some of the most disadvantaged segments of our populations. Women currently account for approximately 24% of homicide deaths (Rosenberg & Fenley, 1991) and 18% of AIDS cases (MMWR, 1995). Understanding the multiple effects of violence on women~s lives, their sexual practices, and substance abuse patterns, can aid in determining the network of women~s HIV risks.

Although many studies document the occurrence of violence in the lives of women at the highest risk of HIV infection, none have empirically established violence as a risk factor of HIV. The complex relationship between women~s risk of HIV and their experiences with violence and substance abuse will form the basis of my research.

1F31MH012050-01
SIBILLE, ETIENNE
NEUROBIOLOGY OF ANXIETY IN 5HT1A KNOCKOUT MICE
WEILL MEDICAL COLLEGE OF CORNELL UNIV
NEW YORK, NEW YORK

DESCRIPTION (Adapted from applicant's abstract): High or excessive anxiety is a major symptom of many neuropsychiatric disorders. The search for anti-anxiety drugs without the side effects of traditional benzodiazepines has led to the discovery of a partial serotonin 1A agonist (buspirone) as an efficient, relatively safe anxiolytic. Recently, 5-HT1A receptor null mutant mice have been generated. These animals display high anxiety-like behaviors and low locomotor activity while appearing otherwise normal. This proposal outlines experiments designed to characterize the molecular, cellular and physiological changes that are the consequences of the receptor deficit and that may underlie this phenotype (Aims 1 and 2). The third aim of this study consists of evaluating the responses of these mice to various anxiolytic drugs in behavioral models of anxiety. A long-term goal is to fully assess the 5-HT 1A receptor knockout mice as putative animal models, not only for screening potential compounds for anxiolytic effects, but also

to decipher the molecular mechanisms that underlie this anxiety trait. Such mechanisms may represent molecular targets for therapeutic approaches.

5F31MH011989-02
SIMERAL, JOHN
NONLINEAR SYSTEMS ANALYSIS OF HIPPOCAMPAL ENSEMBLES
WAKE FOREST UNIVERSITY
WINSTON-SALEM, NORTH CAROLINA

DESCRIPTION (Adapted from applicant's abstract): This research will develop and evaluate nonlinear methods of analyzing information content in spike activity recorded from ensembles of hippocampus neurons in behaving animals. Existing linear algorithms (discriminant analysis) have been used to extract behaviorally-significant information encoded among populations of neurons when firing is time-locked to specific task-relevant events of a short-term memory(DNMS) task (Deadwyler et al., 1966). Nonlinear methods have the advantage of allowing analyses of neuron activity independent of other events in order to detect patterns missed by linear analyses. Detection of neural codes embedded within ongoing ensemble activity not necessarily synchronized to external events will provide a means of "predicting" behavioral responses prior to when those identified linear patterns emerge. The research will adapt Volterra representations of nonlinear systems and draw upon nonparametric optimizations currently in the systems theoretic literature. A computationally-efficient neural network equivalent of Volterra-class systems (three-layer perception)will be adopted for computation of high-order kernel representations of neural firing patterns. Analyses will utilize existing as well as new data recorded from microelectrode arrays implanted in highly trained rats and will initially be evaluated relative to linear discriminant analyses previously published by this laboratory (Deadwyler and Hampson, 1977). The applicant will develop and characterize specific algorithms, a neural network design, and a generalizable nonlinear approach for extracting behaviorally-significant information from populations of hippocampal neurons.

5F30MH011977-02
SIMS, KAREN
REGULATION OF EAAC1, A NEURONAL GLUTAMATE TRANSPORTER
UNIVERSITY OF PENNSYLVANIA
PHILADELPHIA, PENNSYLVANIA

The objective of this proposal is to examine how the activity and cellular localization of the neuronal glutamate transporter subtype EAAC1 is regulated by second messenger pathways. It has become clear in recent years that glutamate acts not only as a neurotransmitter in the normal mammalian brain, but that elevated levels of glutamate are involved in epileptic seizures as well as the excitotoxic neuronal damage that occurs in stroke, acute head trauma, and neurodegenerative disease. EAAC1 is a neuron specific glutamate transporter which is present in high levels in the cortex and the hippocampus. Better understanding of th regulation of EAAC1 may help explain why these areas of the brain are more susceptible to excitotoxic damage and seizure activity. Using the C6 glioma cell line that endogenously expresses EAAC1, the contribution of second messenger pathways to both transport activity and cellular localization will be assessed. Changes in 3[H]- glutamate uptake activity after manipulating these pathways with activators and inhibitors will be performed. Changes in cellular distribution of the transporter may be an additional mechanism for rapidly increasing glutamate uptake, and will be assessed in parallel to uptake studies using biotinylation of cell surface proteins with

subsequent Western analysis and confocal microscopy. To control for more subtle changes in cellular membrane physiology, electrophysiological recordings from voltage clamped cells treated with the same pharmacological agents will be obtained. To better relate the C6 glioma findings to in vivo function, the EAAC1 transport characteristics of neuron enriched rat hippocampal cultures will be analyzed to look for similarities or differences of regulation, and the effects of neuronal EAAC1 upregulation on glutamate toxicity in these cultures will be examined. It is hoped that a better understanding of EAAC1 regulation might provide clues as to how the brain copes with excessive glutamate release in pathological states, if transporter malfunction contributes to neurological damage, and how therapeutic strategies might be used to enhance transporter function in times of excitotoxic stress such as stroke, trauma or chronic disease.

1F31MH012077-01
SMITH, DAVID
NEURAL MEDIATION OF CONTEXT APPROPRIATE BEHAVIOR
UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN
CHAMPAIGN, ILLINOIS

DESCRIPTION (Adapted from applicant's abstract): The overall goal of the proposed research is to identify and characterize the neurophysiological substrates of certain context-appropriate behaviors. Since the learning context plays an important role in normal learning and memory, developing an understanding of the neuronal mechanisms that underlie context-specific behavior is an important step towards understanding how the brain processes information for future use. More specifically, this project seeks to test the hypothesis that the hippocampus signals contextual information to the cingulothalamic system to produce special patterns of neuronal activity that mediate context appropriate associations and behaviors in a discrimination learning paradigm. This will be accomplished by recording the activity of neurons in cingulothalamic circuitry and the behavior of control rabbits and rabbits with temporary and permanent lesions of the hippocampus while they perform two different discriminative learning tasks in different environments.

1F31MH012020-01
SMOKOWSKI, PAUL
RISK AND RESILIENCE IN ADOLESCENT MENTAL HEALTH
UNIVERSITY OF WISCONSIN
MADISON, WISCONSIN

DESCRIPTION (Adapted from applicant's abstract): This study investigates ecological (individual, family, school and community) predictors of positive mental health, using two distinct methods of operationalizing resilience ((1) as a continuous variable and (2) as a categorical construct) across two critical stages of development (middle childhood - age 11 and adolescent - age 16). It compares short- and long-term resilience processes and delineates differential impacts of distal, proximal and multiple concurrent risk factors ("pileup"). Childhood factors associated with the development of adolescent resiliency will thus be delineated for a sample of 850 inner-city, minority youth. The investigation utilizes existing data from the Chicago Longitudinal Study of Children at Risk (acronym CLS: NICHHD grant R29HD34294), a prospective program of longitudinal research focused on the long-term academic and social effects of an early childhood Child Parent Center intervention program.

Aside from delineating resilience correlates, primary study objectives include: A) exploring how childhood risk and resilience is associated with adolescent risk and resilience, B) assessing various types of levels of risk to determine their relative deleterious impacts on mental health and C) evaluating to what extent resilience in one domain is related to resilience in other areas. Sample hypotheses include; 1) proximal risk variables and accumulated risk will have strong, negative main effects in predicting mental health outcomes, 2) protective interaction effects will be found among individual, family, school, and neighborhood variables and 3) resilience will be domain-specific with some domains showing more temporal stability than others. Analyses will use ols linear and multi-nominal logit regression techniques.

1F31MH012047-01
SOBEL, DAVID
CAUSAL EXPLANTATION AND CATEGORIZATION IN DEVELOPMENT
UNIVERSITY OF CALIFORNIA
BERKELEY, CALIFORNIA

DESCRIPTION (Adapted from Applicant's Abstract): While it is well documented that children with autism are impaired in their language development, research on their categorization has shown little to no impairment. However, such research has focused only on children's categorization using perceptual features of objects and not considered what role causality plays in conceptual development. This project seeks to examine conceptual and language development in both normal children and children with autism, focusing on their causal understanding of the world. Furthermore, conceptual development has usually been related to aspects of language development. It is possible that understanding categorization using causal features of objects is related linguistically to providing causal explanations about the world. Children between the ages of 24 months and 6 years will be given categorization tasks that use causal and perceptual cues. They will also be given narrative tasks, designed to elicit explanations about the world. Children with autism of certain ages will also be tested. In this way, we can discover if the linguistic and conceptual developments are linked and what role they might play in diagnosis and treatment.

5F32MH011668-02
SOLOMON, KAREN
NEW INFORMATION EFFECT ON MULTIPLE CATEGORIES
NORTHWESTERN UNIVERSITY
EVANSTON, ILLINOIS

DESCRIPTION (Applicant's Abstract): People and objects can belong to multiple overlapping categories. For instance, a person may be a feminist, a librarian, and a mother. Some information, however, may seem more relevant to one category than to another. For instance, finding out that this person participated in a woman's rights march may cause us to activate and update our category for feminist, but to ignore our categories for librarians and mothers. Thus, not all categories in memory may be activated and updated with new information. But failing to update all possible categories with the new information may reinforce stereotypical beliefs (feminists participate in women's rights movements) and suppress other possible beliefs (librarians participate in women's rights movements). The purpose of the proposed research is to investigate how new information about an entity is understood when the entity is a member of multiple overlapping categories.

5F31MH011516-02
SPENCER, KEVIN
INTERHEMISPHERIC INTERACTION IN ATTENTION
UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN
CHAMPAIGN, ILLINOIS

DESCRIPTION (Adapted from Applicant's Abstract):
This project explores how attention in normal individuals is mediated by the inter- action of the attention systems of the cerebral hemispheres. There is considerable evidence that the hemispheres differ in their attentional characteristics, but it is not known how the single "spotlight" of attention that we experience emerges from the interaction of the hemispheres. This project will help advance our understanding of the relationship between brain and mind, and will ultimately help us to understand the effects of brain damage on cognitive function. Interhemispheric interaction in visuo- spatial attention will be studied with brain event-related potentials (ERPs) and standard behavioral measures. Measurements of ERP components will permit the study of neural systems involved in various types of attentional processing. Measures of "hemispheric utilization bias", which is likely to be an important factor in interhemispheric interaction, will also be used. The proposed experiments examine different aspects of interhemispheric interaction in attention: the processing stages involved, the influence of task difficulty and stimulus probability, trial-to-trial switching, and the shifting of attention. Through this research, we aim to develop a model of how attention is mediated by interhemispheric interaction.

1F31MH012053-01
SPIEGEL, SCOTT
ACCESSIBILITY EFFECTS IN A UNIMODAL THEORY OF PERSUASION
UNIVERSITY OF MARYLAND COLLEGE PK CAMPUS
COLLEGE PARK, MARYLAND

DESCRIPTION (Applicant's abstract): The present research will test aspects of a unimodal theory of persuasion that emphasizes the epistemic similarities between processing message-related and non-message-related (e.g., speaker expertise) information. Previous research has demonstrated that increasing the accessibility of a heuristic cue such as "length implies strength" increases the degree to which people who are uninvolved in a topic use such a cue in a persuasion setting. The current research will attempt to demonstrate that making the premises of message-based information more accessible can also result in increased use of this information for uninvolved message recipients. These findings could have important theoretical and empirical implications. Theoretically, they would demonstrate that heuristic and message-based information are identically affected by accessibility. Specifically, both types of information would benefit from increased accessibility more under low versus high involvement on the message recipients' part. On an applied front, the findings of this research could have implications for public campaigns advocating healthier behavior and obtaining compliance on the part of individuals seeking treatment in personalized settings. Specifically, this research would suggest that making either cue or argument premises more accessible would induce greater compliance on the part of the typically uninvolved targets of such campaigns. For example, priming targets early in a broadcast advertisement with the values "living a long, healthy life" or "being a good

parent for my children" might increase the effectiveness of arguments against smoking and alcohol abuse respectively.

1F31MH012037-01
SRINIVASAN, RAJAGOPAL
IMAGE ENCODING BY THE PRIMATE LATERAL GENICULATE NUCLEUS
EMORY UNIVERSITY
ATLANTA, GEORGIA

DESCRIPTION (Adapted from applicant's abstract): The proposed research in sensory coding is a necessary first step in a rigorous approach to understanding how the visual signals that encode real visual scenes are transformed into the physiological correlate of perception or awareness. The proposed research aims to: 1) develop a novel experimental method for decoding and interpreting neural activity in individual channels of the primate lateral geniculate nucleus (LGN); 2) evaluate a simple nonlinear model of precortical visual processing that explains the results obtained in (1) using just the principles of monotonicity and differentiation, two common properties of precortical neurons in many sensory systems including the visual system. The proposed experiments will be performed in rhesus monkeys, a practical model for human perception. The monkey model will also expedite the use of experimental results in the design of visual-neural prosthetic devices aimed at restoring sight in humans.

5F31MH011792-02
STARK, JENNIFER
NGF MODULATION OF VIRUS INDUCED INFLAMMATION
OHIO STATE UNIVERSITY
COLUMBUS, OHIO

DESCRIPTION (Applicant s Abstract): It has been demonstrated in animal models and in humans that the hormones released during chronic stress can increase both an individual s susceptibility to viral infections and the pathology of an on-going infection. Specifically, stress elevates blood levels of glucocorticoids (GCs), which down-regulate the expression of cellular adhesion molecules and pro-inflammatory cytokines. These actions inhibit the normal mononuclear cells. However, recent data from the candidate's laboratory show that social reorganization (SRO) stress enhances lung inflammation in a murine model of influenza infection, despite the fact that plasma GCs are significantly elevated. This stressor disrupts the established dominance hierarchy among the mice, and elicits aggressive behavior. Fighting between male mice has been reported to elevate serum levels of nerve growth factor(NGF), and the NGF may mediate the observed inflammation in two majors ways: by stimulating lymphocytes via specific receptors and by counter-acting the anti-inflammatory actions of GCs at a cellular and/or molecular level. The candidate will test the hypothesis that lymphocyte GC receptors are down-regulated during SRO. In addition, the specific role of NGF in the progression of influenza infection will be determined in vivo by removing the source of NGF (salivary glands) prior to SRO and infection. These studies aim to advance the understanding of the mechanisms by which stress can modulate the regulation of an immune response and negatively affect host health.

5F30MH011388-03
STINE, CHRISTY
GLUTAMATE TRANSMISSION IN A RAT MODEL OF SCHIZOPHRENIA
FINCH UNIV OF HLTH SCI/CHICAGO MED SCH
CHICAGO, ILLINOIS

DESCRIPTION (Applicant s Abstract):
Two important clinical observations about schizophrenics are not accounted for by most animal models: 1) typical onset of symptoms just after puberty, and 2) structural abnormalities in the hippocampal formation, possibly due to early developmental injury. A novel rat model of schizophrenic, in which neonatal rats receive excitotoxic lesions of ventral hippocampus (VH), yields rats which appear normal until puberty, but then exhibit behavioral abnormalities which model schizophrenic symptoms in humans. This model will be used to study the role of excitatory amino acid (EAA) transmitters in schizophrenia. An important role for EAAs in schizophrenia is indicated by reports that both EAA receptor expression and EAA levels are altered in schizophrenic brains and in rat brains following subchronic administration of antipsychotic drugs. Proposed studies will determine if changes in EAA receptors or levels accompany postpubertal onset of symptoms in VH-lesioned rats, focusing on medial prefrontal cortex and nucleus accumbens. Aims are: 1) In vivo microdialysis will compare basal and K-stimulated EAA levels in VH- and sham-lesioned rats, 2) In situ hybridization histochemistry will be used to quantitatively examine mRNA levels for AMPA and NMDA receptor subunits in VH- and sham-lesioned rats. 3) Autoradiographic immunocytochemistry will examine the same subunits at the protein level. 4) Rats will be prescreened for response to novelty to correlate magnitude of behavioral and EAA abnormalities. For Aims 1-3, it will be determined whether any observed changes are normalized by subchronic haloperidol or clozapine. Results should provide information about the possibility that developmentally-induced abnormalities in EAA transmission contribute to schizophrenia.

1F31MH012234-01
TAFT, CASEY
PREDICTING DROPOUT AND CHANGE IN BATTERERS TREATMENT
UNIVERSITY OF MARYLAND BALT PROF SCHOOL
BALTIMORE, MARYLAND

DESCRIPTION (Applicant's Abstract): The broad, long-term objective of the proposed project is to gain a better understanding of the factors which contribute to positive therapeutic change and treatment completion among domestic abusers in a cognitive-behavioral treatment program. Specifically, the effects of personality variables (antisocial and borderline characteristics), referral source (court or self-referred), social factors (interpersonal problems), the motivation of the patient (states of change), the relationship between the therapist and the patient (working alliance), and treatment adherence will be examined. Approximately 140 male domestic abusers and their partner will be assessed at three time periods, with additional ratings of the working alliance and homework compliance/treatment involvement conducted during the treatment phase. Multiple regression will be the primary data analytic method utilized to address three specific aims: (1) to determine factors that lead to the formation of a working alliance in treatment, and examine the interrelationships among these variables; (2) to investigate the influence of the working alliance and stages of change on treatment outcomes and dropout rates, and to uncover intervening factors in these relationships; and (3) to examine racial differences in working alliance formation.

1F31MH012091-01
TALLEY, EDMUND

ANTIDEPRESSANT EFFECTS--CELLULAR/MOLECULAR MECHANISMS
UNIVERSITY OF VIRGINIA
CHARLOTTESVILLE, VIRGINIA

DESCRIPTION (adapted from the applicant's abstract): SSRIs are an important class of antidepressants that are believed to produce their therapeutic effects by enhancing serotonergic transmission. The fact that there is a two-to-four week delay in their efficacy suggests that their benefits depend on long-term adaptive changes in the central nervous system. One of the long term effects that are thought to be crucial to SSRI treatment is the downregulation of an autoinhibitory mechanism mediated by 5-HT1A receptors on 5-HT-synthesizing raphe neurons. The autoinhibitory mechanism is well described, involving direct coupling between the 5-HT1A receptor, a heterotrimeric G-protein, and a G-protein-coupled inwardly-rectifying potassium (GIRK) channel. However, in spite of the attention it has received, the specific cellular and molecular events responsible for the SSRI-induced down-regulation of this autoinhibition remain obscure. The proposed research will use ligand binding autoradiography and whole-cell voltage clamp recordings in an in vitro slice preparation to determine the locus of regulation of this mechanism. In addition, in situ hybridization will be used to determine whether the observed down-regulation results from SSRI-induced alterations in expression of genes coding for the proteins constituent to this transduction pathway. Specific Aims: 1) Determine effects of chronic SSRI treatment on 5HT1A receptor-G protein coupling in dorsal raphe neurons; 2) Determine effects of chronic SSRI treatment on G protein-GIRK channel coupling in dorsal raphe neurons; 3) Determine effects of chronic SSRI treatment on 5HT1A receptor and GIRK channel mRNA levels in dorsal raphe neurons.

5F32MH011145-03
TAN, PHILIP
SORTING OF A MEMBRANE PROTEIN INTO LDCVS
SCRIPPS RESEARCH INSTITUTE
SAN DIEGO, CALIFORNIA

DESCRIPTION (Adapted from applicant's abstract): Communication between cells in the nervous system depends on the regulated release of signaling molecules. In contrast to synaptic vesicles which store classical transmitters, the large dense core vesicle (LDCV), a component of the regulated secretory pathway, stores neural peptides and hormones. Monoamine transmitters are also stored in LDCVs, further indicating the importance of this secretory pathway for major mental illness and drug abuse. The long term objective of this proposal is to understand how the storage of these neuromodulators contributes to information processing and psychiatric disease. The strategy is to use a transporter that packages monoamines into vesicles to understand the biogenesis of LDCVs and the regulated secretory pathway. Proteins destined for the regulated pathway sort away from constitutively released proteins at the level of the trans-Golgi network (TGN) but the mechanism remains unknown. Presumably, sorting involves the specific interaction of integral membrane proteins destined for the LDCV with a cytosolic sorting machinery. The laboratory has recently shown that a vesicular amine transporter (VMAT2)preferentially localizes to LDCVs rather than constitutive secretory vesicles or synaptic-like microvesicles and so provides the first opportunity to study this important sorting event directly. In the first specific aim, we will use deletions and then point mutations to identify signals on VMAT2 required for sorting to LDCVs. To complement this approach and determine whether these sequences are sufficient for targeting to LDCVs, the second

specific aim examines chimeras with another closely related transport protein that does not sort to LDCVs. The results of this work will provide some of the first information about the mechanism of sorting into the regulated secretory pathway and has important implications for the release of hormones, neural peptides and growth factors as well as monoamine transmitters.

5F32MH011417-02
TANNENBAUM, PAMELA
SOCIAL REGULATION OF REPRODUCTIVE ENDOCRINOLOGY
UNIVERSITY OF WISCONSIN
MADISON, WISCONSIN

DESCRIPTION (Adapted from Applicant's Abstract):
Female common marmoset monkey reproductive capacity is completely regulated by social status. Subordinate females show no ovarian activity and have low levels of pituitary gonadotropins, yet hypothalamic gonadotropin-releasing hormone (GnRH) output is not different when compared to cycling dominant females. The present study will systematically examine neuroendocrine parameters at several points along the hypothalamic-pituitary-gonadal axis in order to characterize any subtle differences between social states. Results will identify mechanisms by which psychosocial factors can influence reproductive integrity through small variations, rather than dramatic global changes, in the neuroendocrine environment.
In all studies GnRH and luteinizing hormone (LH) parameters will be measured and compared between dominant, rank 2 and rank 3 females. Females will undergo push-pull perfusion of the stalk-median eminence with concomitant blood sampling at 10 min intervals for up to 10 hr. Experiment 1 will look for altered diurnal patterns hypothalamic GnRH and pituitary LH release. Experiment 2 will characterize GnRH and LH responses underlying the ability or inability to generate an ovulatory LH surge in response to estradiol. Experiment 3 will examine differential pituitary stimulation and responsiveness to standardized GnRH challenges; GnRH receptor concentrations will be quantified.

1F31MH011771-01A2
TAYLOR, AMY
MENTAL MODEL OF FUN AND IMPORTANCE INFLUENCE PERFORMANC
COLUMBIA UNIV NEW YORK MORNINGSIDE
NEW YORK, NEW YORK

DESCRIPTION (Applicant's abstract): The proposed research is designed to explore the effects of attributions of fun, importance, and combinations thereof as reasons for engagement activities. Established social-psychological paradigms are employed to test the hypothesis that actors have mental models of motivations for engaging in activities, and drawing on Mandler's (1975) model of the disruptive motivational effects of 'disconfirmed expectancies', performance will be better when the instructional framing for engaging in a particular activity matches versus mismatches the mental model of the actor for that activity. The proposed experiments are designed to test this hypothesis for activities pre-determined to be: "just fun"; "just important"; "primarily fun but also important"; "primary important but also fun"; and "equally fun and important". Consensual mental models for a set of activities will first be examined, controlling for the actual nature of the task. Then individual differences in mental models for the same activity will be investigated. This research program could help to improve individuals' performance on

different activities and increase their desire to perform the activities in the future. The mental health implications are manifold, suggesting interventions that would improve individuals performance and subjective well-being. Theoretically, the proposed research is designed to extend our understanding of how motivational attributions can combine in a number of ways to influence performance depending on contextual framing.

5F31MH011650-02
TEKIRIAN, TINA
ENTORHINAL CORTEX PATHOLOGY AND COGNITIVE PERFORMANCE
UNIVERSITY OF KENTUCKY
LEXINGTON, KENTUCKY

DESCRIPTION (Adapted from Applicant's Abstract):
Alzheimer's disease (AD), a progressive neurodegenerative disorder which causes memory loss and dementia, is characterized by the presence of neuritic plaques and neurofibrillary tangles in select brain regions. Several observations suggest that pathology in entorhinal cortex play critical roles in the development of dementia. However, it is contentious whether tangles or plaques (and beta-amyloid deposits) in this region correlate with dementia. This proposal will examine the relationship between entorhinal pathology and cognitive function using data and tissues obtained from the Nun Study, a longitudinal study of aging in 678 Catholic Sisters. Preliminary studies demonstrate that both beta-amyloid load (% area occupied by beta-amyloid deposits) and neurofibrillary pathology in entorhinal cortex correlate with cognitive decline. The first specific aim will extend these observations, and examine specific beta-amyloid isoforms as well as the relationship between the beta-amyloid deposits and neurofibrillary pathology. The second specific aim will examine specific hypotheses regarding the relationship between plaques and tangles. Tangles contain paired helical filaments, composed of hyperphosphorylated tau. We predict that beta-amyloid itself does not cause tau hyperphosphorylation, but rather leads to tau dephosphorylation. Neuritic plaques are associated with activated microglia, which release cytokines including tumor necrosis factor and interleukin-1. These proinflammatory cytokines inhibit phosphatase activity in fibroblasts. This proposal will examine the hypothesis that TNFalpha and IL-1alpha mediate phosphatase inhibition which contributes to tau hyperphosphorylation in entorhinal neurons.

5F30MH011649-03
TENG, EDMOND
HIPPOCAMPUS--SPATIAL AND NONSPATIAL MEMORY FUNCTION
UNIVERSITY OF CALIFORNIA
SAN DIEGO, CALIFORNIA

DESCRIPTION (Adapted from applicant's abstract): The long-term objective of this research is to provide a clearer understanding of the role the hippocampal region plays in memory function. This is a particularly important health related issue because this region of the brain is critically important for memory, yet is vulnerable to damage in various pathological conditions, including those associated with stroke, aging, and Alzheimer's disease. The applicant proposes to examine the effects of specific lesions restricted to the hippocampal region on performance on the delayed nonmatching to sample(DNMS) task and the delayed recognition span task (DRST). The specific aims related to the study are: 1) to determine whether the hippocampal region has a special role in spatial memory and 2) to determine whether damage limited to the hippocampal region that includes damage to white matter fibers

produces the same effects as damage limited to the hippocampus that spares white matter fibers. These aims will be accomplished by preparing two groups of monkeys with bilateral lesions limited to the hippocampal region that spare the cortical components of the medical temporal lobe memory system (the entorhinal, perirhinal, and parahippocampal cortices). One group will receive radio frequency lesions and the other group will receive ibotenate lesions. The two groups of operated monkeys and one group of normal control monkeys will be tested on spatial and nonspatial versions of the DNMS and DRST tasks to determine whether the hippocampal region plays a disproportionate role in spatial memory and whether the behavioral effects of lesions of the hippocampal region are dependent on damage to the white matter fibers in the region.

5F32MH011549-02
THOMPSON, RICHMOND
NEUROPEPTIDE INFLUENCES UPON SEXUAL BEHAVIOR
OREGON STATE UNIVERSITY
CORVALLIS, OREGON

DESCRIPTION (Adapted from applicant's abstract): The present proposal will elucidate the potential mechanisms by which the neuropeptide argininevasotocin (AVT) affects the expression of sexual behavior in male roughskin newts. It is hypothesized that this molecule exerts its behavioral influence by acting as a central neuromodulator and influencing responsiveness to specific sexual stimuli. This will be tested by measuring behavioral and electrophysiological responses toward sexual stimuli presented within isolated sensory modalities (e.g., visual, chemosensory, somatosensory) in response to brain AVT manipulations. Additionally, the AVT neural pathways involved in generating this neuropeptide's effects upon sensory responsiveness will be determined. These studies will advance our understanding of the mechanisms by which neuropeptides influence the expression of behavior in vertebrate animals, perhaps even in our own species.

5F31MH010721-03
TOMA, DANIEL
MOLECULAR GENETIC ANALYSIS OF BEHAVIOR
UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN
CHAMPAIGN, ILLINOIS

DESCRIPTION (Adapted from applicant's abstract): The objective of this project is to contribute to an understanding of the molecular genetic basis of behavior. To achieve this objective, the following hypothesis will be tested: specific patterns of gene expression are associated with specific behavioral states in the honey bee (Apis mellifera). This will be addressed by studying genetic expression in the bee brain during post-embryonic behavioral development. Animals will be collected at three discrete stages of normal post-embryonic behavioral development: day-olds, brood care (nursing), and foraging. Comparisons of gene expression will be accomplished using the "differential display" technique. RNA will be isolated from the brain and cDNA copies will be made using specific primers. These will be amplified by PCR and compared on a sequencing gel. Differentially expressed putative cDNAs will be used to generate digoxygenin-labeled probes. These will be used to screen a cDNA bee brain library to recover a larger and higher quality fragment representing the expressed gene. To confirm that the gene is differentially expressed during different behavioral states, RNA dot blots of brain tissue from bees exhibiting the relevant behaviors will be performed using a probe made from the library insert cDNA. In addition, by using RNA on

the dot blots from brain tissue of animals behaviorally accelerated, retarded, or reverted at similar states, it can be determined whether differences in gene expression are related to differences in behavior rather than age (nurses are typically younger than foragers). If differences are reliably associated with behavior, the gene will then be sequenced, and I will attempt to determine function by looking for homologies to genes already in Gen Bank, insitu whole mounts for region-specific expression, and developmental northerns for timing of expression. In the event that behaviorally relevant genes cannot be found with the above methods, a cDNA library of bee brains will be probed with Drosophila genes that have been implicated in regulating behavior. Genes that can be used are per genes, dunce, biogenic amine receptor genes, and certain immediate early genes, such as c-fos. If found, these genes will be used to probe dot blots of behaviorally staged bees, outlined above, to see if they are involved in post-embryonic behavioral development. It is hoped that results from these experiments will provide insight into the neural and genetic mechanisms of an organism's ability to cope with environmentally influenced changes.

1F31MH011958-01A1
TREUTING, JENNIFER
PATHWAYS TO DEPRESSIVE SYMPTOMS AMONG CHILDREN WITH ADHD
UNIVERSITY OF CALIFORNIA
BERKELEY, CALIFORNIA

DESCRIPTION (Adapted from applicant's abstract): ADHD represents a large proportion of all diagnosed child psychopathology and those with ADHD suffer from both core ADHD symptoms and a range of secondary difficulties. Although increased risk for depressive symptoms has been documented among ADHD children, little research has directly explored mechanisms linking these two areas of difficulty. Research on childhood depression has identified a number of child- and family-level risk factors, including maternal depression, critical parenting, aggressive behavior, and peer rejection. Interestingly, each of these risk factors has also been independently linked to ADHD. However, the degree to which these risk factors account for elevated depressive symptoms among ADHD children remains unclear. This paucity of research is surprising given that children with co-occurring internalizing (e.g., depression) and externalizing (e.g., ADHD) problems are at high risk for severe negative outcomes (e.g., suicidality). Here, I propose a model of child depressive symptoms and, through naturalistic summer camps, evaluate the utility of this model in predicting depressive symptoms among children with and with ADHD. Two moderational models serve as comparisons to the primary mediational model. Long-term goals of this research are increased understanding of (a) the development of depression among children, (b) mechanisms placing ADHD children at risk for poor outcomes, and (c) variables key to well-informed prevention and treatment.

1F31MH012289-01
TSAI, HOUNG
MECHANISM FOR ABOLISHING GONADOTROPIN SURGES BY ESTROGEN
UNIVERSITY OF KENTUCKY
LEXINGTON, KENTUCKY

DESCRIPTION (applicant's abstract): The long term goal of this proposal is to elucidate the neuroendocrine mechanisms responsible for reproductive dysfunction in aging female rats at the systemic, cellular and molecular

levels. It remains to be determined whether chronic exposure to preovulatory estradiol (E2) levels causes loss of the LH surge-inducing actions of E2 that occur in aging rats, and if so by what mechanism. This proposal will focus on the role of estrogen receptors (ER) in the medullary noradrenergic neurons tha project to the hypothalamic luteinizing hormone-releasing hormone (LHRH) neurons in mediating the loss of the positive feedback action of E2. The specific aims are to test the hypothesis that chronic exposure of ovariectomized (OVX) rats to preovulatory levels of E2: (1) causes a sequentia loss of the LH surge-inducing actions of E2 and P; (2) suppresses the gene expression of estrogen receptor (ER) in the NE neurons that project near the LHRH perikarya; (3) decreases the number and/or proportion of ER immunopositiv NE neurons; and (4) alters the in vivo pattern of NE release. The proposed studies will determine the effect of E2 on changes in plasma LH concentrations by radioimmunoassay, dialysate NE levels by high pressure liquid chromatography, ER-alpha and -beta m/RNA levels by in situ hybridization, and immunocytochemical localization of ER-alpha and -beta in noradrenergic neurons The results of these studies should increase our understanding of the mechanisms whereby E2, which plays an important role in mental health, alters brain function.

5F30MH011607-02
TURNER, MICHAEL
PALLIDAL GLUTAMATE IN A RAT MODEL OF PARKINSONS DISEASE
LOYOLA UNIVERSITY MEDICAL CENTER
MAYWOOD, ILLINOIS

DESCRIPTION (Adapted from applicant's abstract): The affective and cognitive symptoms of PD pose a significant problem in the field of mental health. These symptoms could result from STN hyperactivity, causing increased EAA release and EAA desensitization in the VP. If cholinergic neurons, which govern cognitive functions, are preferentially sensitive to AMPA, and GABAergic neurons, which influence affective states, are preferentially sensitive to NMDA, then perhaps specific therapy can be directed toward each sub-population. We hypothesize that changes consistent with increased EAA neurotransmission occur in the VP following a substantia nigra lesion. In a rat model of PD with a unilateral 6-hydroxydopamine (6-OHDA)-induced lesion of the substantia nigra, we will compare left and right pallidal regions to test the following hypothesis in three Specific Aims. Hypothesis 1: Dopaminede afferentation will increase spontaneous neuronal activity and decrease sensitivity to EAA agonists in the VP. Neuronal firing will be measured by extracellular single neuron electrophysiology. Microiontophoresis of receptor subtype-selective EAA agonists and antagonists will be used to measure EAA sensitivity and endogenous EAA-induced spontaneous firing, respectively. Hypothesis 2: dopamine deafferentation will reduce EAA-evoked c-fos/c-junexpression in the VP, and will differentially alter EAA receptor subtype-selective agonist-evoked c-fos/c-jun expression between cholinergic and GABAergic neurons. Expression of c-fos/c-jun will be induced by microinjection of EAA receptor subtype-selective agonists into the VP. C-Fos/c-jun and markers for cholinergic or GABAergic neurons will be detected by immunofluorescence. Hypothesis 3: Destruction of neurons in the STN will tend to normalize the changes in spontaneous neuronal activity and EAA-induced effects in the VP caused by dopamine deafferentation. Neurons in the STNipsilateral to the lesioned substantia nigra will be destroyed with ibotenicacid and the procedures outlined for Specific Aims 1 and 2 will be repeated.

5F30MH010819-04
TYRKA, AUDREY
NEUROPSYCHOLOGICAL INDICATORS OF RISK FOR SCHIZOPHRENIA
UNIVERSITY OF PENNSYLVANIA
PHILADELPHIA, PENNSYLVANIA

DESCRIPTION (Adapted from candidate's application): The candidate's primary interest is in academic psychiatry and neuroscience; she is committed to conducting research, teaching, and having clinical responsibilities. Her areas of specific interest are neuroanatomy, neurophysiology, and genetics of mental illness, particularly schizophrenia. The candidate's curriculum provides a balance between basic sciences including electives in other graduate groups such as genetics and neuroscience, coursework in psychology, teaching experience, and independent research. Her research in the departments of psychology and psychiatry will include developing further facility with neuropsychological testing, magnetic resonance imaging, positronemission spectroscopy, behavioral symptom rating, behavioral genetics, and statistical modeling with regard to schizophrenia.

5F31MH011776-02
VAIDYA, MANISH
DO EQUIVALENCE CLASSES MEDIATE EXTENSIONS OF FUNCTION?
UNIVERSITY OF FLORIDA
GAINESVILLE, FLORIDA

DESCRIPTION (adapted from applicant's abstract): The specific purpose of the proposed research is to gain a better understanding of the role of stimulus equivalence in the extension of stimulus functions to novel stimuli. To the extent that such extension of function is characteristic of symbolic functioning, the broad aims are to gain a greater understanding of how such competencies arise, are maintained, and participate in the organization of human behavior. The research proposed in this application will determine whether equivalence classes 1) are necessary for the extension of stimulus functions and 2) mediate the maintenance of such extensions. Experiment 1will train and assess equivalence class formation and the extension of stimulus functions simultaneously, allowing a more precise characterization of the relationship between the two phenomena. The extension of stimulus functions after equivalence class formation would suggest that equivalence classes mediated the transfer whereas observed transfer of function prior to equivalence class formation would call the mediating role of equivalence classes into question. The second experiment will determine whether equivalence relations among stimuli mediate the maintenance of extended stimulus functions by changing equivalence relations among stimuli. A change in stimulus functions following a realignment of the equivalence relations would suggest that equivalence classes continue to mediate the extension of stimulus functions. No change in functions may suggest that the two kinds of activity can become independent of one another.

1F31MH011763-01A2
VALERA, EVE
MINOR HEAD INJURY IN BATTERED WOMEN
UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN
CHAMPAIGN, ILLINOIS

DESCRIPTION (adapted from applicant's abstract): The purpose of this study is twofold: (1) to estimate the incidence of minor head injury (MHI) in battered women, and (2) to examine the effects of MHI on battered

women's cognitive and psychosocial functioning. Battered women exhibit a variety of problems including cognitive disturbances such as memory, attention, and concentration problems. These problems are also commonly seen in individuals who have sustained MHIs. Although researchers in the domestic violence field have anecdotally suggested that MHIs play a role in the problems experienced by battered women, no one has systematically examined this hypothesis. This study will test this hypothesis by using neuropsychological methods to assess battered women. Responses on neuropsychological, psychological, and abuse severity measures will serve to gauge cognitive and other possible effects of MHIs on battered women's functioning. The importance of this research lies in its potential to increase the effectiveness of treatment, legal services, and social services provided for victims of violence.

5F31MH011465-02
VERIN-SHAPIRO, PENNY
RELIGIOUS HEALING AND IDENTITY IN PUERTO RICO
CASE WESTERN RESERVE UNIVERSITY
CLEVELAND, OHIO

DESCRIPTION (Adapted from Applicant's Abstract):
This comparative anthropological ethographic study examines the cultural meaning of religious healing for Puerto Ricans in the rural island town of Yauco. It examines the relation of religious healing and identity with respect to religious participation, social class, ethnicity and nationality. It will thus contribute to the understanding of how important Puerto Rican social themes are articulated as problems in need of religious healing. The study will examine events of religious healing identified with Catholicism, Pentecostalism, Espiritisemo (Spiritism), Santeria (worship of saints/African deities) and Vodoun. The events of religious healing will be compared with respect to a) problems needing healing; b) experiences of healing; and c) social traits of participants. It is proposed that the symbolism deployed in these events will be found to constitute national, political, and ethnic as well as religious identity among participants. This research will help mental health practitioners in Puerto Rico and the U.S. understand why people participate in religious healing. This may help practitioners become more open to and understanding of patients using religious healing alone or with biomedicine. This will show that religious healing may be used to define and express identity and well as heal .

1F31MH011886-01A1
VICKBERG, SUZANNE
ADJUSTMENT TO BREAST CANCER--THE ROLE OF INTERPRETATION
CUNY GRADUATE SCH AND UNIV CTR
NEW YORK, NEW YORK

DESCRIPTION (Adapted from the Applicant's Abstract): The goal of the proposed research is to understand factors that may influence women's interpretations of breast cancer experience, namely personal beliefs and interpersonal relationships. A study using both qualitativive and quantitative methods is proposed. Approximately 140 breast cancer survivors will complete standardized paper and pencil questionnaires assessing psychological adjustment, interpretation of the breast cancer experience (including causes, consequences, and controllability), personal beliefs, and interpersonal relationships. Twenty of the respondents will then participate in a semi-structured qualitative

interview, focusing on the same issues. Specific aims of the proposed study are: 1) to determine whether any particular aspect of interpretation is better predictor of psychological adjustment than the others; 2) to identify factors that may influence women's interpretations of breast cancer, specifically personal beliefs and interpersonal relationships; and 3) to test a model in which interpretations mediate the association of personal beliefs and interpersonal relationships to adjustment.

1F32MH012186-01
VNEK, NORBERT
FUNCTIONAL MODULARITY OF THE PRIMATE PREFRONTAL CORTEX
YALE UNIVERSITY
NEW HAVEN, CONNECTICUT

DESCRIPTION (Adapted from applicant's abstract): Over the course of the last twenty years much has been learned about how the architecture of the primate prefrontal cortex (PFC) gives rise to working memory functions. For example, there is now evidence suggestive of a topographic representation of the visuospatial world in the PFC. However, the precise nature of this topographic map remains elusive, as the methods traditionally used to study structure function relationships in the PFC do not have the requisite spatial or temporal resolving power to uncover it. The studies described here are designed to apply optical imaging methodology, a powerful technique that has been widely used to map functions in primary and association sensory cortical areas to examine functional topography in primate PFC. Optical recordings of the PFC will be conducted in monkeys as they perform the oculomotor delayed response (ODR) task to map the functional organization of the PFC. The activation maps generated by optical recordings will be used to guide electrode penetrations for electrophysiological characterization of functional modules. We will then examine the extrinsic and intrinsic connectivity of functional PFC modules by injecting anterograde and retrograde tracers into different regions shown by optical and electrophysiological recordings to be related to specific parameters of the ODR task. Through adaptation of optical imaging methods to the study of awake, behaving animals, the proposed project promises to reveal the topography of the visuospatial memory functions that are housed in the primate PFC.

1F31MH012011-01A1
VOLLRATH, MELISSA
HAIR CELL TRANSDUCTION IN A MAMMALIAN VESTIBULAR ORGAN
BAYLOR COLLEGE OF MEDICINE
HOUSTON, TEXAS

DESCRIPTION (Adapted from applicant's abstract): About 40 percent of Americans over 40 complain of dizziness at some time. In many cases, loss or damage of sensory cells in the inner ear is implicated. Dysequilibrium negatively impacts quality of life and productivity and can lead to depression and anxiety. Much remains unknown about the normal function of sensory cells in mammalian vestibular organs, which provide the input to reflexes that maintain balance and gaze. I propose to study stimulus processing by sensory cells in the mouse utricle. Hair cells, the sensory receptors of the inner ear, contain voltage and mechanically gated conductances that interact to shape the signals sent to the central nervous system. The mouse utricle contains two types of hair cells distributed throughout the organ. These cells are contacted by three types of

vestibular afferents whose discharge properties vary systematically with the region of the utricle they innervate. The mechanisms underlying this regional organization are unknown, but are likely to include regional differences in the voltage and mechanically gated channels of hair cells. How the expression, voltage ranges of activation, or adaptation kinetics of these conductances vary is not known. Preliminary data show variations among utricular hair cells in ion channel expression, voltage ranges of activation and adaptation kinetics, but whether these or other differences are regionally organized is not known. This proposal aims to investigate whether hair cell properties vary with region and whether the differences observed explain differences in afferent firing properties.

1F31MH012176-01
WAINWRIGHT, MARCY
MORPHOLOGICAL CORRELATES OF LONG TERM SENSITIZATION
UNIVERSITY OF TEXAS HLTH SCI CTR
HOUSTON, TEXAS

DESCRIPTION (Adapted from applicant's abstract): One of the fundamental problems in neurobiology is to understand the cellular and molecular events underlying learning and memory. Considerable progress has been made in understanding the neural basis of simple forms of learning in the marine mollusk, Aplysia, through the study of two simple defensive withdrawal reflexes, tail siphon withdrawal and gill siphon withdrawal. These reflexes can be modified by sensitization, a simple form of non-associative learning in which the behavioral response to a mild stimulus is enhanced following the presentation of another, usually noxious, stimulus. Previous studies suggest that one general correlate of sensitization is the modification of neuronal structure. However, this assumption may be oversimplified. Preliminary studies suggest that there may be multiple forms of long-term sensitization, and that morphological changes are only induced by the more present forms of this memory. The specific aims of this research project are: 1) to determine the time course of long-term sensitization in the tail induced siphon withdrawal reflex; 2) to determine the conditions that induce a form of long-term sensitization associated with morphological changes; and 3) to examine the functional role of neuronal outgrowth in long-term sensitization. The effects of various training protocols on both the behavioral response of the reflex, and on the morphology of the sensory neurons mediating this response will be analyzed. Changes in neuronal morphology will be analyzed using 3-D reconstructions of the neuronal structure. In addition, we will use confocal microscopy to examine whether neuronal outgrowth is contributing to the behavioral response by strengthening pre-existing connections to motor neurons, or by adding new connections to the neuronal circuitry underlying the response. Through the quantitative analysis of neuronal morphology we hope to provide a more complete framework for a structural model of learning and memory.

1F31MH012125-01
WALTZ, JAMES
INVESTIGATING REASONING DEFICITS IN DEMENTIA PATIENTS
UNIVERSITY OF CALIFORNIA
LOS ANGELES, CALIFORNIA

DESCRIPTION (Applicant's abstract): The proposed project is designed to investigate the nature of reasoning impairments in dementia of Alzheimer's type, and related disorders. In addition, by integrating neuropsychological data with brain imaging data, the study seeks to determine the roles of

different brain regions in reasoning. The performance of three groups of patients will be compared on tests of working memory, declarative memory, and reasoning: 1) a group of patients with focal damage to prefrontal cortex, 2) patients with damage limited to anterior regions of temporal cortex, and 3) patients with damage to posterior cortical areas, producing dementia of Alzheimer's type. A group of age-matched control subjects will also be tested. Items from reasoning tests systematically vary in the number of relational representations they require reasoners to simultaneously manipulate. It is proposed that intact prefrontal cortex is essential for successful reasoning because it is required for the integration of relations between objects and events. Thus, it is hypothesized that patients with damage to prefrontal cortex will show significant impairment, relative to patients with Alzheimer's disease, on items which require relational integration. Additionally, it is predicted that a double dissociation will be found between relational reasoning and declarative memory abilities in patients with damage to prefrontal cortex and patients with Alzheimer's Disease. Finally, I hypothesize that significant correlations will be observed between scores on measures of working memory and relational reasoning in all participant groups.

1F31MH012182-01
WARD, BONNIE
BRAIN SPACE AND AVIAN VOCAL LEARNING
UNIVERSITY OF ROCHESTER
ROCHESTER, NEW YORK

DESCRIPTION (Adapted from applicant's abstract): The hypothesis that brainspace constrains learning potential is not easily testable in most systems due to the lack of dedicated neural network for a single behavior. In songbirds, such a dedicated series of nuclei exist, thus facilitating direct investigation of brain/behavior relationships. Both across species and among individuals of several species, repertoire size is positively correlated with the size of song nucleus, the HVc. In zebra finches not only HVc volume, but also the number of HVc neurons predicts how much song material is accurately reproduced. We propose a three-tier approach to better understand the relationship between network space and learning potential. First, retrograde tracing will be used to identify the neuronal subpopulations within the HVc responsible for the correlation to learning. Because only a subset of these cells are added during song learning, this information will provide insight into which stages of learning may be limited by HVc neuron number, as well as further define the role of the different pathways in song learning. Second, we will begin to explore variables that might generate the tremendous variation in HVc neuron number by determining if it covaries with clutch order and/or yolk concentrations of testosterone. Finally, we will use microinfusions of the neurotrophin bFGF to increase the number of HVc neurons, testing the causality of the observed relationship. This work has broad implications for understanding the biological processes that regulate individual learning capacity.

1F31MH012132-01
WEBB, SARA
ONTOGENY OF MEMORY--ELECTROPHYSIOLOGICAL EVIDENCE
UNIVERSITY OF MINNESOTA TWIN CITIES
MINNEAPOLIS, MINNESOTA

DESCRIPTION (Applicant's Abstract): Ontogeny of Implicit Memory: Electrophysiological Evidence Studies with adults suggest that there are

multiple memory systems, yet little is known about how this neurocognitive organization develops. This is unfortunate because any valid theory of memory must account for how the system matures and organizes. Specifically, researchers have proposed that implicit memory might be a functionally "earlier" developing system than explicit memory. In order to study the ontogeny of implicit memory, we propose to use event-related potentials (ERPs) with infants at 4-, 6-, and 8-months on a repetition priming paradigm. Priming occurs when a prior exposure to a stimulus affects how that stimulus is processed and interpreted at a later time. Changes in the timing or topography of electrocortical activity due to changes in repetition patterns will allow us to assess the different psychological factors that may influence memory performance. Moreover, this paradigm allows us to measure changes in cognitive activity without requiring any over behavioral responses by the infant. In order to facilitate our understanding of the development of implicit memory, adult participants will be run on a comparable paradigm.

5F31MH011779-02
WEERSING, VANESSA
THERAPY PROCESS CHECKLIST--DEVELOPMENT AND APPLICATION
UNIVERSITY OF CALIFORNIA
LOS ANGELES, CALIFORNIA

DESCRIPTION (Adapted from applicant's abstract): The proposed study is the centerpiece of a program of research to establish the psychometric properties of the Therapy Process Checklist (TPC). The TPC is being developed to measure child and adolescent psychotherapists' technique use and etiologic beliefs in order to aid our efforts to understand the mediators and moderators of child therapy effectiveness. Completion of the TPC will also provide the field with a new research tool--a measure of child psychotherapy process with evidence on reliability and validity. As explicated in the specific aims, the psychometric properties of the TPC will be delineated using a sample of practicing child and adolescent psychotherapists whose clients are participants in a longitudinal investigation of child therapy effectiveness. Demographic and therapy outcome data will be available for these children, and, as a second component of this proposal, research uses of the TPC will be illustrated, including tests of whether therapy processes measured with the TPC relate to changes in child functioning one year after psychotherapy.

5F30MH011697-02
WEIHL, CONRAD
VIRAL VECTORS IN THE STUDY OF ALZHEIMERS DISEASE
UNIVERSITY OF CHICAGO
CHICAGO, ILLINOIS

DESCRIPTION (Adapted from applicant's abstract): This is a 6-year MD/PhD predoctoral fellowship application from Conrad Weihl to conduct his training and research program at the University of Chicago Pritzker School of Medicine. Familial Alzheimer's Disease (FAD) has recently been associated with mutations in a novel class of presumed transmembrane proteins known as presenilins (presenilins-1 (PS-1) and presenilins-2 (PS-2)) (1,2). Currently, the only insight into the functions of PS-1 and PS-2 is amino acid sequence homology to C elegans gene products sel-12 (approximately 50% identity) and spe-4 (approximately 26% identity). Therefore, experimentation to elucidate the functions of mutant and wild type (WT) presenilins in neurons and live animal models would be valuable; unfortunately, transfection of neurons is very inefficient and no animal model is presently available. In order to overcome

these limitations, the investigators plan to express WT and mutant PS-1 andPS-2 in primary cultured hippocampal neurons (HNs) and in the central nervous system (CNS) using recombinant replication-deficient adenoviruses (AdVs) as vectors, and to determine the effects of this expression on morphology, viability, physiology, and production of pathologic features and proteins associated with Alzheimer's disease (AD). Studies in the central nervous system (CNS) will involve gene delivery via stereotaxic injection in the hippocampus as well as nasal instillation of the virus. In addition, they will use AdVs that encode cDNAs for B galactosidase: tetanus toxin c fragment(LacZ: TTC), and cell physiological techniques (e.g., patch clamping).Finally, during the in vivo experimentation, the candidate will develop skills in animal handling and central nervous system tissue isolation. His goal is not only technical proficiency, but the capability of knowing "when" and "why" to use these skills in neurobiological investigation. The candidate indicates that while neuroanatomy and pathology have taught him the structural framework of the CNS, he currently lacks training in neurobiological physiology and neuronal systems. Hence, in order to foster his knowledge base in neurobiology, he is enrolled in several graduate neurobiology courses. The contact that he will have with his mentor and his colleagues is aimed at enriching his knowledge in these areas. Heightening his understanding of basic neurobiology, aims to give him the resources in which to pose questions and explore answers which are vital to success as a researcher.

5F31MH011762-02
WEST, JENNIFER
CHILDREN AND MARITAL CONFLICT--LINKS TO SOCIAL BEHAVIOR
UNIVERSITY OF DENVER
DENVER, COLORADO

DESCRIPTION (Adapted from applicant's abstract): The goal of the proposed research is to examine how exposure to parental violence operates within the context of additional risk factors (low socioeconomic status, maternal depression, lack of mother-child relationship positivity, major life stressors) and with children's aggressive expectations in peer relationships in the relation between exposure and children's social behavior. The aforementioned risk factors, aggressive expectations, severity and duration of violence witnessed, aggressive behavior problems, and social competencies of 150 children from violent homes will be compared to those of a community group of children where conflict ranges from verbal discord to low level aggression and does not include violence. Parents, shelter counselors, and teachers will complete several measures regarding family violence and their child's functioning, mothers will complete additional measures assessing their degree of depressive symptomatology and their perceptions of mother-child relationship positivity, and children will complete several measures assessing their aggressive expectations in peer relationships, mother-child relationship positivity, and their perceptions of warmth and conflict in their close peer relationship. This research has implications for improving models of the processes through which parental violence impacts on development and for informing prevention and intervention strategies to help child witnesses adjust to their experiences.

5F31MH011972-02
WETHERELL, JULIE
GENERALIZED ANXIETY DISORDER IN OLDER ADULTS
UNIVERSITY OF SOUTHERN CALIFORNIA
LOS ANGELES, CALIFORNIA

DESCRIPTION (Adapted from applicant's abstract): The proposed study is a randomized clinical trial of group-administered cognitive behavioral therapy(CBT) for generalized anxiety disorder (GAD) in older adults. The design compares arm to an attention placebo (discussion group) and a wait list control group at pre-, post-1 and six-month follow-up assessment periods. Both treatment conditions will take place 90 minutes weekly for 12 weeks. The SET condition will include relaxation training, cognitive restructuring, and worry exposure. Outcome measures will include subjective and interviewer-rated symptoms of anxiety and worry, depression, health-related quality of life and health service use, and physiological correlates of anxiety(frontalis electromyogram and salivary cortisol under baseline and stress conditions). CBT participants are expected to show greater reductions in show improvements in health outcomes and greater maintenance of treatment gains at the six-month follow-up period.

1F32MH012100-01
WILLCUTT, ERIK
BEHAVIORAL AND MOLECULAR GENETIC STUDY OF ADHD
UNIVERSITY OF COLORADO
BOULDER, COLORADO

DESCRIPTION (Adapted from Applicant's Abstract): The proposed research will utilize behavioral and molecular genetic techniques to examine the etiology of DSM-IV Attention Deficit/Hyperactivity Disorder (ADHD) in a sample of 100 8-13 year old twins selected because at least one twin meets the criteria for ADHD. Univariate behavioral genetic models will be utilized to estimate the genetic and environmental components of the etiology of the subtypes of ADHD. In addition, bivariate behavior genetic analyses will be utilized to directly examine the influence of common genes on the three proposed subtypes and the etiology of any observed psychiatric comorbidity with ADHD. DNA samples will be obtained from all DZ twins and their families. Association analyses such as the Transmission Disequilibrium Test will be utilized to test whether any component of the ADHD phenotype is significantly associated with any of several theoretically plausible candidate genes. In addition, a bivariate interval mapping linkage analysis will be utilized in a sample of individuals already typed for the relevant markers to test whether a previously mapped quantitative trait locus for reading disability on chromosome 6 is also etiologically related to ADHD.

5F32MH011563-02
WILLIAMS, JULIE
MELATONIN FUNCTION IN CIRCADIAN RHYTHMS
MASSACHUSETTS GENERAL HOSPITAL
BOSTON, MASSACHUSETTS

DESCRIPTION (Adapted from Applicant's Abstract):
Melatonin has been shown to affect circadian rhythms in mammals, including humans, and has been used in therapeutic applications such as treating jet lag and some sleep disorders. However, the mechanisms by which melatonin exerts its effects are not well understood. In order to address this issue, the specific aim of the research proposal is to investigate the mechanism by which melatonin resets the circadian pacemaker. Based upon the behavioral effects of melatonin observed in mammals, we hypothesized that melatonin acts to suppress light signals in the suprachiasmatic nucleus (SCN), which is known to be the anatomical substrate for the mammalian circadian clock. Using whole-cell patch clamp and molecular

biological techniques this hypothesis will be tested by studying the effects of melatonin on the membrane properties as well as on intracellular effector molecules in SCN neurons. Determining the signal transduction pathways triggered by melatonin is key to defining its function in circadian rhythms.

1F31MH012121-01
WILSON, JULIE
HUMAN NEURAL SYSTEMS FOR PERCEIVING EMOTION IN MUSIC
UNIVERSITY OF IOWA
IOWA CITY, IOWA

DESCRIPTION (Applicant's abstract): The primary aim of the proposed study is to investigate the neuroanatomical systems involved in perceiving emotion in music. Few studies have investigated the neural systems involved in music perception in general, and none have specifically investigated the neural systems for perceiving emotion in music. Neuropsychological and functional imaging studies implicate amygdala and right parietotemporal cortices in perceiving emotion in facial expressions and in prosody. Here, it is predicted that damage to these structures will impair perception of emotion in music. This prediction will be tested by comparing ratings of emotional music given by subjects who have lesions in target regions with ratings given by control subjects. To control for other auditory perceptual impairments, subjects' hearing thresholds and discrimination of simple melodies and rhythms will be measured. To determine if regions of the brain necessary for perceiving emotion in music are distinct from regions necessary for perceiving emotion in other types of stimuli, individual subjects abilities to perceive emotion in music will be compared to their abilities to perceive emotion in nonverbal sounds, prosody, and facial expressions. A large number of subjects (n=68) with focal brain lesions will be studied, and advanced three-dimensional lesion analysis techniques will be used to correlate damage to specific anatomical structures with impairments on experimental tasks. The findings will improve understanding of neural systems that subserve emotion and music perception, and they will inform strategies for treatment of patients with neurologic or psychiatric diseases that cause disorders of emotion or higher-level auditory function.

5F32MH011489-02
WILSON, WILLARD
LOCALIZATION AND TRACKING OF MOVING TARGETS BY BATS
UNIVERSITY OF MARYLAND COLLEGE PK CAMPUS
COLLEGE PARK, MARYLAND

DESCRIPTION (Adapted from applicant's abstract): Most mammals depend on their ability localize moving sound, and echolocating bats are an excellent example of the importance of accurate auditory localization in the presence of motion. Microchiropteran bats use a biological sonar system to navigate through their environment and capture insect prey on the wing. Echolocation by bats in flight therefore produces dynamic auditory space both from the stationary environment, and from flying prey. Accurate auditory spatial processing by bats must consequently be carried out in a dynamic environment. Behavioral analysis of the response to moving sound by the big brown bat, Eptesicusfuscus, is proposed here in an attempt to gain new insight into the mechanisms used to process, utilize, and resist potential localization errors produced by auditory motion. Two sets of experiments are proposed, the first being a determination of head and pinna aim of otherwise stationary bats trained to orient toward moving inanimate targets. The second set of

experiments will consist of behavioral analysis of insect captures while the bat is echolocating in flight. The focus of these experiments is to: 1) Determine the behavioral orienting response of the head and external ears to moving sound. 2) Determine how sound motion affects the ability to accurately localize a moving sound. 3)Ascertain the strategies used by echolocating bats to intercept moving targets. 4) Apply these data to elucidate common principles of sensorimotorintegration across different species and modalities.

5F31MH011831-02
WINNIER, ANGELA
MOLECULAR GENETICS OF THE NEURAL SPECIFICITY GENE BKN-1
VANDERBILT UNIVERSITY
NASHVILLE, TENNESSEE

DESCRIPTION (Adapted from applicant's abstract): Neural function depends on The creation of synaptic connections between specific sets of neurons. Despite the importance of this phenomenon, the molecular cues that instruct Neurons to synapse with appropriate target cells are unknown. Mutations in The C. elegans unc-4 homeodomain gene alter target selection in a specific Motor neuron circuit. The backing again-1 (bkn-1) gene was identified in a Screen for mutations that suppress the unc-4 movement defect and is therefore a candidate for a gene that is either regulated by unc-4 or which is required for unc-4 transcriptional activity. The goal of this proposal is to molecularly define the bkn-1 gene in order to distinguish between these models of bkn-1 action. The specific aims are as follows: (1) Clone the bkn-1 locus. Bkn-1 will be cloned using microinjection/rescue assays with cosmids which cover the bkn-1 region. (2) Molecular analysis of bkn-1. The bkn-1 sequence will be compared to known database proteins, and bkn-1 mutant alleles will be sequenced. (3) Analysis of bkn-1 expression. Specific antibodies will be generated to localize BKN-1 expression. The dependendence of bkn-1 expression on unc-4 activity will be evaluated. (4) Isolation of new bkn-1 alleles. Additional bkn-1 alleles will facilitate our analysis of bkn-1 function.

1F31MH012124-01
WINTERBAUER, NANCY
STRESS AND CULTURE CHANGE AMONG THE YUCATEC MAYA
STATE UNIVERSITY NEW YORK BINGHAMTON
BINGHAMTON, NEW YORK

DESCRIPTION: (Applicant's abstract): This study will examine the biological response to acculturative stress in the context of profound and rapid social change. The field-setting for this project is the eastern coast of the Yucatan Peninsula, Mexico. Since the early 1970's, this area has undergone a massive, planned development in response to a growing international tourism industry. As such, many indigenous Yucatec Maya have been drawn into the world economy. In the resort environment, gender, social, and work roles are especially vulnerable to change (Daltabuit 1994; Thomas and Pi-Sunyer 1994; Pi-Sunyer and Thomas 1997), with resultant challenges to mental and physical well-being. However, little work, either in anthropology or psychology, has addressed within-population variation in the biological response to acculturative stress. This project builds on previous work on the relationship between culture change and biology (measured through blood pressure and heart rate, urinary catecholamines, plasma cortisol and antibodies to Epstein-Barr virus-an indirect measure of immune function) by explicitly addressing intracultural variation in the stress response. Particular attention is

paid to sex-differences in the definition of, and response to, psychosocial stress; the effect of group normal on the individual stress response, and the causal relationship between psychosocial stress, immunity, and infectious disease in a natural setting.

1F32MH012244-01
WISOR, JONATHAN
DOPAMINE & SLEEP HOMEOSTASIS--MOLECULAR GENETIC APPROACH
STANFORD UNIVERSITY
STANFORD, CALIFORNIA

DESCRIPTION (applicant's abstract): The Compensatory Sleep Response (CSR; characterized by increased sleep time and depth) that is seen in mice after a period of total sleep deprivation (TSD) indicates that sleep is a homeostatic process. The mechanism for this homeostatic drive is unknown, but is likely to be involved in the etiology of some sleep disorders. We have found that simila to TSD, methamphetamine, an inhibitor of the cell membrane dopamine (DA) transporter (DAT) and of the intracellular DA transporter (VMAT2), produces sleep loss followed by a CSR in mice. In contrast the DAT-specific inhibitor GBRI2909 produces sleep loss without a subsequent CSR. In light of these observations we theorize that intracellular DA stores play a critical role in sleep homeostasis. This proposal addresses three issues relevant to this theory. Is the wake promoting effect of OBR12909 mediated exclusively through inhibition of DAT9? Are the wake promoting effect of methamphetamine and the subsequent CSR mediated through inhibition of DAI and of intracellular DA stores? Do genetic alterations of cell membrane (DAT) and vesicular (VMAT2) DA transporters alter CSR to TSD? We propose a targeted molecular genetic approac to address these questions. To determine the molecular sites of action of GBRI2909 and methamphetamine, we will study the effects of these drugs on slee in mice with genetic alterations of DAT and VMAT2 expression. To determine the role of DAT and VMAT2 in physiological sleep in the absence of pharmacological manipulation, we will also study the CSR to TSD in these genetically engineere mice.

5F31MH011815-02
WOLF, ROBERT
PSYCHOSOCIAL DETERMINANTS FOR HIV RISK BEHAVIORS
JOHNS HOPKINS UNIVERSITY
BALTIMORE, MARYLAND

DESCRIPTION (Applicant's Abstract): The candidate's particular interest in The field of public health is behavioral research on AIDS prevention. While There have been some long-awaited breakthroughs in drug development, with the Protease inhibitors, they are still not a cure for HIV disease. Prevention Education and intervention programs remain essential to slow the spread of Transmission of HIV. The candidate would like to carry out research on Primary prevention to identify and evaluate AIDS-interventions. Toward this Goal, the candidate plans to use data from quantitative and qualitative Sources to measure changes in HIV knowledge, beliefs, and behaviors, and to Determine societal factors which may be barriers to prevention efforts. The Intervention components which the investigator is interested in assessing may Include: individualized HIV/AIDS risk assessment, peer education and risk Reduction counseling, support groups, referrals to needed services, and use of Mass media. The investigator is interested in multi-level interventions which Modify risk behavior norms in individuals, groups and communities at various

Stages of change.

5F31MH011279-02
WOODS, ALISA
NEUROCYTOKINES IN REACTIVE HIPPOCAMPAL SPROUTING
UNIVERSITY OF CALIFORNIA
IRVINE, CALIFORNIA

DESCRIPTION (Adapted from Applicant's Abstract):
Reactive hippocampal sprouting in response to entorhinal cortex lesion demonstrates the ability for continued growth in the adult brain and can be used to identify mechanisms used by the brain to compensate for lost synapses. The mechanisms directing hippocampal sprouting are unknown. Interleukin-1beta (IL-1beta) and basic fibroblast growth factor (bFGF) increase in the hippocampus following entorhinal cortex lesion. We have recently demonstrated that the mRNA for insulin-like growth factor-1 (IGF-1) and ciliary neurotrophic factor (CNTF) increases in response to entorhinal Cortex lesion, with a spatial and temporal correspondence to the sprouting response. The goal of the proposed research is to evaluate if these growth factors collaborate to promote sprouting in the adult rat brain. This will be accomplished by (i) determining if CNTF protein is increased by deafferentation, (ii) testing if CNTF, IGF-1 or bFGF increases c-fos or tyrosine phosphorylation in commissural/associational neurons in vitro, (iii) testing if IL-1beta can regulate the gene expression of IGF-1 or CNTF in vitro, and (iv) determining if CNTF, IGF-1 or bFGF promote sprouting in the organotypic slice preparation alone or synergistically. These studies will extend our knowledge of trophic factors that facilitate axonal plasticity in brain may suggest endogenous mechanisms of compensation for brain damage.

1F32MH011793-01A1
WOTRING, VIRGINIA
KINETIC ANALYSIS OF WILD-TYPE/MUTANT GABA RHO RECEPTORS
UNIVERSITY OF ALABAMA
BIRMINGHAM, ALABAMA

DESCRIPTION (adapted from the applicant's abstract): GABA regulates neural excitability and is known to be involved in a number of brain disorders including epilepsy. Therapeutic agents that modulate GABA receptors are currently used for sleep disorders, depression, mood disorders, and control of seizures, yet their mechanisms of action on the receptor are not well understood. As a basis for understanding these diseases and developing therapies, it is necessary to first elucidate the mechanism of GABA's interaction with its receptor. In order to do this, the GABA rho receptor, which forms a functional homomer, will be exogenously expressed in HEK cells and examined with electrophysiological methods. Chimera that switch portions of rho1 and rho2, as well as point mutations, will be constructed in order to determine the domains that are involved in receptor activation. Currents elicited by GABA will be measured and dose-response relationships of both wild-type and mutants will be determined. Regions that play a role in channel activation will be isolated by construction of progressively smaller chimera and point mutations. The single channel kinetics of wild type and select mutants will be studied to gain insight into the activation mechanism as well as the mechanism by which the mutations impair activation. The results from this project will lead to a better understanding of the structural domains and activation mechanism of the GABA receptor.

5F32MH011462-02
WRAGA, MARYJANE
EYE HEIGHT AND SIZE PERCEPTION
UNIVERSITY OF VIRGINIA
CHARLOTTESVILLE, VIRGINIA

DESCRIPTION (Applicant's Abstract): Observer eye height (EH)--the point at which one's line of gaze intersects an object or scene--is a readily accessible source of information that can be used to scale the sizes of objects in the environment. In principle, this is accomplished by forming a ratio of the object's total height with the portion of it that falls below the intersection with observer EH. The purpose of this research is to investigate factors governing the utility of EH in perceiving size. Three main factors will be addressed. The first is the size of the object relative to the observer. There is obviously an optimal range of object sizes for which observer EH is used: The proposed experiments will delimit this range. The second factor is the posture of the observer. If EH scaling is a common strategy for gauging object size, then it ought to be accessible from different postures, such as sitting. The proposed experiments will determine whether and how EH is used in different postural contexts. The third area of study is environmental constraints; specifically, the assumption of common level ground between observer and object. Perturbing this relationship by having subjects judge object size on a slope (i.e., standing on a hill) will establish the efficacy of EH scaling independent of the natural horizon. Inmost studies, the use of EH will be explicitly tested by manipulating it unbeknownst to subjects. This will be accomplished in two ways: 1)introduction of a false floor into the field of view; and 2) the use of Virtual Reality (VR). In all experiments, within-subjects' size judgments of rectangular objects in EH-manipulated and unmanipulated conditions will be compared.

1F32MH012111-01
WRIGHT, TIMOTHY
DISCRIMINATION OF NATURAL AND SYNTHETIC CALL VARIANTS
UNIVERSITY OF MARYLAND COLLEGE PK CAMPUS
COLLEGE PARK, MARYLAND

DESCRIPTION (Adapted from applicant's abstract): This study will examine the perception of natural and synthetic communication calls by two parrot species. Categorical perception is considered to occur when continuously varying stimuli are perceptually classified into a discrete group and there is increased discriminability of variants across categorical boundaries. In this project, three separate experiments will test whether either the yellow-nape amazon or the budgerigar 1) has categorical perception of yellow-nape amazon vocalizations, and if so 2) whether both species perceive similar categories in the same set of calls. The first experiment will test the basic auditory sensitivities of the yellow-nape amazon and compare them to available audiograms for the budgerigar and other bird species. The second experiment will compare the abilities of the two species to discriminate among novel variants of natural calls of the yellow-nape amazon and test whether either species has perceptual categories that correspond to previously defined acoustic categories. The third experiment will compare the abilities of the two species to discriminate between equally spaced synthetic variants and test for the existence of the sharp boundaries in discriminability between variants characteristic of categorical perception. In sum, these experiments will begin to address two general questions: first, whether natural calls are perceived in a categorical fashion by

animals and, second, whether these categories are species-specific (restricted to a species own calls) or are general (found for both conspecific and heterospecific calls). The proposed project will provide valuable training in methods for signal synthesis, acoustic analysis, and psychoacoustical testing. It will also contribute to the development of a model system with great potential for the study of auditory perception and vocal learning.

1F30MH012066-01
WU, GREGORY
CTL ESCAPE MUTANTS--ROLE IN MHV INDUCED DEMYELINATION
UNIVERSITY OF IOWA
IOWAS CITY, IOWA

DESCRIPTION (Applicant's Abstract): The candidate's goal in joining the neuroscience graduate degree program from medical school has been to integrate clinical knowledge of human disease with basic science research. The training component of the Ph.D. phase will enable the candidate to conduct independent research in a career that one day will hopefully include both clinical and laboratory responsibilities. The interdisciplinary nature of the neuroscience program provides experience in molecular, cellular, and systems neuroscience. The project, involving the pathogenesis of viral-induced demyelination, affords the opportunity to learn a great deal about molecular biology, immunology and virology, and combine them with neuroscience. This integration of various disciplines will be valuable in pursuing neuroscience research and clinical applications in the future. In terms of the project itself, information with mouse hepatitis virus, strain JHM (MHV-JHM), a neurotropic coronavirus, results in acute encephalitis and chronic demyelination. The latter serves as a model for the human demyelinating disease, multiple sclerosis. In the proposed model, a variable percentage of MHV-infected mice are protected from an otherwise fatal acute encephalitis but later develop a chronic demyelinating encephalomyelitis with clinical signs of hindlimb paralysis. Previous results suggested that the development of clinical disease several weeks after inoculation was in part due to the selection of cytotoxic T-cell (CTL) escape mutants. The goal of this proposal is to determine more definitively whether CTL escape mutants contribute to the pathogenesis of chronic demyelination. In order to achieve this, three specific aims will be undertaken: (1) To determine whether infection with variant virus results in the development of chronic demyelination at earlier times after inoculation and with a higher frequency; (2) To assess the role of the subdominant CD8+ T-cell epitope (epitope S-598-605) in viral persistence and chronic demyelination; and (3) To determine why only a subset of all possible mutations in the immunodominant CD8+ T-cell epitope S-510-518 are selected during persistent infection. Mice persistently infected with MHV-JHM serve as a model system for analyzing the significance of CTL escape mutants and their relevance to the pathogenesis of demyelination.

5F31MH011375-02
WU, MARK
MUTATIONAL ANALYSIS OF SYNTAXIN 1-A IN VIVO
BAYLOR COLLEGE OF MEDICINE
HOUSTON, TEXAS

DESCRIPTION (Adapted from Applicant's Abstract):
The goal of this research proposal is to develop a better understanding of the mechanisms underlying neurotransmitter release. Syntaxin-1A is a

conserved presynaptic membrane protein that has been shown to be essential for exocytotic release of synaptic vesicles. Syntaxin is thought to mediate its function through its interactions with other proteins involved in neurotransmitter release. In addition to these interactions, phosphorylation of syntaxin may potentially play a critical role in regulating syntaxin's function in neurotransmitter release, as is the case for other synaptic proteins, such as synapsin. This work proposes to perform a mutational analysis of syntaxin 1-A in Drosophila to identify amino acids or regions that are critical for its function in vivo. To perform this analysis, targeted mutagenesis will be performed on syntaxin-1A in Drosophila to generate systematic regional deletions and point mutations that may disrupt syntaxin's interactions with other proteins and disrupt specific phosphorylation sites. The importance and function of these regions and amino acids will be assessed by observation of mutant flies, electrophysiological analysis and in vitro binding assays. The dissection of the function of syntaxin-1A in vivo through electrophysiological and biochemical analysis should yield important insights into the mechanisms of synaptic vesicle release. Understanding this mechanism could provide a framework for addressing issues such as drug action at the synapse disease states associated with changes in neurotransmitter release, and the processes underlying learning and memory.

1F31MH011660-01A2
WURTS, SARAH
CIRCADIAN AND HOMEOSTATIC REGULATION OF REM SLEEP
STANFORD UNIVERSITY
STANFORD, CALIFORNIA

DESCRIPTION (adapted from applicant's abstract): The proposed experiments will investigate how the circadian system regulates the expression of rapid-eye-movement (REM) sleep. This work offers new basic understanding of REM sleep physiology relevant to the clinical significance of REM sleep disturbances in depression, schizophrenia, narcolepsy, alcoholism, obsessive-compulsive disorder, and Alzheimer's disease. REM sleep has a robust circadian rhythm and appears to be homeostatically regulated in rodents and humans. Although the circadian pacemaker located in the suprachiasmatic nucleus of the hypothalamus (SCN) is thought to promote cortical and behavioral activation and oppose compensatory NREM sleep drive, it is not known how the circadian system interacts with compensatory REM sleep mechanisms. Furthermore, the essential neural connections between the SCN and the REM sleep generator in the brain-stem have not been identified. The experiments in this revised pre-doctoral NRSA proposal will investigate how circadian and homeostatic influences may be integrated to shape REM sleep by: (1) comparing the compensatory REM sleep responses of intact and SCN-lesioned rats to REM sleep deprivation at different circadian times, and (3) examining the convergence of SCN/proximal relay efferent and dorsal raphe afferent projections with FOS and glutamic acid decarboxylase (GAD67) immunohistochemistry in the vlPHA after REM sleep deprivation and compensation.

5F31MH011761-02
YARALIAN, PAULINE
PSYCHOPHYSIOLOGY--AGGRESSION AND HYPERACTIVITY
UNIVERSITY OF SOUTHERN CALIFORNIA

DESCRIPTION (Adapted from applicant's abstract): The proposed study will investigate how the predictive relationship between autonomic under arousal and later antisocial behavior is affected by additional factors such as the comorbidity of two disorders, social adversity, gender, and ethnicity. Measures of skin conductance and heart rate taken at age 3 will be compared in four groups of children: hyperactive and antisocial, antisocial only, hyperactive only, and normal controls at ages 8 and 16. It is hypothesized that children who are both antisocial and hyperactive will demonstrate the lowest levels of arousal. This relationship is hypothesized to be consistent across diverse ethnic groups, but stronger in female antisocials and antisocials from benign homes where the social predisposition towards crime will be weaker. The applicant is located in the Psychology Department at UCLA and her sponsor is Dr. Adrian Raine. The applicant plans to increase her knowledge and skills in psychophysiological recording procedures, longitudinal research design, and advanced data analytic techniques. The training plan includes coursework and seminars in addition to the research project, and writing manuscripts for publication.

5F32MH011390-03
YECKEL, MARK
ACTIVE PROPERTIES OF DENDRITES OF CA3 PYRAMIDAL NEURONS
BAYLOR COLLEGE OF MEDICINE
HOUSTON, TEXAS

DESCRIPTION (Adapted from applicant's abstract): Thus far the research efforts have focused on the functional relation between monosynaptic and multisynaptic excitation of the hippocampus by entorhinal afferents. Based on the results of these studies the applicant has proposed a re-conceptualization of the intrinsic circuitry of the hippocampus: monosynaptic entorhinal input to CA3 and CA1 provides feed forward modification of activity propagating through the trisynaptic pathway. The aim of the project is to investigate the cellular mechanisms that underlie observations showing that the nature and extent of the feed forward modification is dynamic, changing as a function of the pattern of entorhinal input. More specifically, it is proposed to test the hypothesis that synaptic activation of voltage-gated ion channels in CA3 pyramidal dendrites provide a fundamental mechanism by which these neurons integrate signals from multiple subsets of synapses such that occurs with direct, monosynaptic excitation by entorhinal afferents and indirect, disynaptic excitation via the mossy fiber projection. To accomplish this, the applicant will use techniques recently developed in the laboratory, including, dendrite-attached patch-clamp recording and high-speed fluorescent imaging. The specific aims are: 1) Characterization of presumed voltage-dependent Ca2+ and Na+ channels in CA3 pyramidal dendrites, evoked by synaptic excitation and/or propagation of action potentials from the soma; 2) Characterization of the functional dynamics of these ion channels when excited by a specific subset of synapses, using different stimulation parameters, including those known to induce short- and long-term changes in synaptic strength; and 3)Characterization of the functional dynamics of voltage-activated currents in CA3 dendrites under conditions that mimic physiological activity, such that might occur when multiple subsets of synaptic are excited, or when different patterns of action potentials are evoked in the soma. The possibility that these interactions might underlie the induction and expression of different forms of long-term potentiation (LTP) will also be examined.

5F32MH011599-02
YEH, MAY
SERVICE DELIVERY TO ASIAN AMERICAN YOUTHS

CHILDREN'S HOSPITAL RESEARCH CENTER
SAN DIEGO, CALIFORNIA

DESCRIPTION (Adapted from Applicant's Abstract):
The proposed project is designed to provide a broad training experience in mental health services with a substantive research focus upon current patterns of mental health service delivery to Asian-American children and adolescents. Documenting current patients of use and investigating influences upon utilization would contribute to empirically-based decisions for and scientific information regarding culturally-responsive service delivery to the traditionally underserved Asian-American youth population. Aim 1 is to document and help understand current patterns of use for Asian-American youths across a broad range of social service agencies. This will be achieved in conjunction with a large grant that provides access to a large population of youths (N=6500) entering mental health services, child welfare, substance abuse treatment programs, juvenile detention centers, and classes for Seriously Emotionally Disturbed children Aim 2 is to supplement an existing service utilization instrument for use with the Asian-American youth population. Interviews and focus groups with service providers will aid the interpretation of these patterns. Aim 3 is to generate testable hypotheses for what strategies are useful in servicing Asian-American youths. Collaboration with an ethnically-specific mental health services center will produce service provider information regarding barriers to and facilitator of service use.

1F31MH012135-01
YU-ISENBERG, KRISTINA
COMPLIANCE WITH ANTIRETROVIRAL THERAPY IN HIV+ WOMEN
JOHNS HOPKINS UNIVERSITY
BALTIMORE, MARYLAND

DESCRIPTION (Adapted from Applicant's Abstract): This 4-year predoctoral request proposes to evaluate data tapes from the HIV Cost and Services Utilization Survey and supplemental Mental Health Study, to evaluate the psychosocial, demographic and illness variables on the prevalence of HIV medication compliance among HIV-infected women. The doctoral training at the John Hopkins University School of Hygiene and Public Health will help prepare the applicant for a career in health services research. She is interested in the use of pharmaceuticals in the respective fields of AIDS and mental health, and more specifically, the impact on patient outcomes. She is currently enrolled in the second term of the first year of doctoral training.
Women represent the fastest growing population of the AIDS epidemic, with rates doubling every 1 to 2 years (CDC, 1996). As of June 1997, women accounted for 15 percent of the total cumulative number of persons with AIDS (CDC 1997). Compared to men with AIDS, women with AIDS are more likely to be poor, minority, intravenous drug users, and exposed through heterosexual contact (Mays and Cochran, 1988; CDC, 1996). Although HIV-infected men and women differ in these characteristics, previous research in the area of medication adherence has been conducted primarily in HIV-positive gay men, raising questions about the generalizability of the findings to women. The dissertation research will be a prospective, longitudinal study to examine the extent to which variables influence compliance in HIV-infected women. Specifically, the specific aims are to: 1) Determine the prevalence of medication compliance with antiretroviral therapy among HIV-infected women; 2) Assess the roles of depression, illness variables,and demographics that impact compliance; and 3) Assess change in compliance over time. Data from

the HIV Costs and Services Utilization Survey (HCSUS) and the supplemental mental Health Study will be analyzed to test the research hypotheses. HCSUS is the first national probability study of HIV patients and medical providers (AHCPR, 1997). It will collect medical and non-medical utilization and costs data on 3300 HIV-positive persons in 28 urban and five rural areas in the United States over 18 months. The Mental Health Study will collect prevalence, access, and quality data pertaining to psychiatric disorders among HIV-infected individuals. Medical, pharmaceutical, and psychiatric records will be abstracted for the dissertation research. Data from these two studies will become available in 1998 through public use tapes for interested researchers.

5F32MH011641-02
ZALD, DAVID
NEURAL CORRELATES OF EMOTION
UNIVERSITY OF MINNESOTA TWIN CITIES
MINNEAPOLIS, MINNESOTA

DESCRIPTION (Adapted from applicant's abstract): Two PET studies are proposed to elucidate the specific contributions of the OFC and amygdala in olfactory and hedonic processing in humans. Study 1 examines whether activity in the amygdala, OFC and pyriform cortex varies in a concentration dependent manner. Fifteen subjects will be exposed to four concentrations of butanol and four concentrations of phenylethyl alcohol while rCBF is measured with PET. Study 1 also examines whether attention modulates rCBF in these regions by imaging subjects while attending to and ignoring odorants. In Study 2, 25 subjects will be exposed to highly aversive pleasant and neutral stimuli to examine if rCBF in the OFC and amygdala varies with the hedonic meaning or emotional responses induced by odorants. These studies represent the first steps in a research program aimed at elucidating the functions of the OFC and amygdala in humans, with a long-term goal of determining the role of these structures in normal and abnormal emotional behavior.

5F31MH011676-02
ZEDDIES, DAVID
ADAPTATION IN RECEPTOR POTENTIALS OF INNER HAIR CELLS
NORTHWESTERN UNIVERSITY
EVANSTON, ILLINOIS

DESCRIPTION (Adapted from applicant's abstract): A model of the inner hair cell in the mammalian hearing organ (cochlea) has been developed whose major components are based on physiological data. This model has given us insights into questions of mental health such as mechanisms of sensorineural hearing loss and sensory adaptation in the cochlea. With sensorineural hearing loss, the model predicts that, in the presence of a prolonged stimulus, sodium ions entering through potassium channels in the hair cell can overwhelm active transport and lead to loss of the cell's osmotic regulation. Concerning sensory adaptation, receptor potentials, the membrane potential's response to stimuli, generated by the model show adaptive behavior at the onset and offset of the stimulus (similar to a phenomenon seen in the auditory nerve).Receptor potentials recorded in vivo using sharp microelectrodes typically do not show this behavior, and it is likewise absent in simulations if a conductance that models the shunt due to microelectrode impalement is included. In the model, the shunt alters the electrical response of the cell by linearizing the basolateral membrane conductance and allowing the membrane potential to depolarize (up to levels reported in in vivo studies) which changes the kinetics of the voltage regulated K+ channels. To test for adaptation

occurring in inner hair cell receptor potentials, simulated transducer currents will be delivered to inner hair cells of an in vitro tissue preparation via the patch-clamp technique in current clamp mode.

1F31MH012167-01
ZEINEH, MICHAEL
FUNCTIONAL MRI OF THE HUMAN HIPPOCAMPUS
UNIVERSITY OF CALIFORNIA
LOS ANGELES, CALIFORNIA

DESCRIPTION (Adapted from applicant's abstract): The goal of this project is to better define the functional anatomy of the human hippocampus in memory processing with fMRI. This project proposes to perform high-resolution structural imaging studies of the hippocampal region, examining activity in the CA fields, subiculum, and entorhinal cortex throughout the anterior-posterior axis bilaterally, during performance of several memory paradigms in normal volunteers. Using computational techniques, the applicant will unfold the hippocampus to provide a flattened functional map of its activity. This research aims to elucidate the functional organization of substructures within the hippocampus in the intact brain. This knowledge will also impact the understanding and treating of diseases involving the hippocampus such as Alzheimer's disease and temporal lobe epilepsy.
There will be three phases to this research: 1) The technology will be developed and optimized for the high-resolution imaging and segmentation of the hippocampus. 2) Stimulus paradigms will be developed with the goal of achieving differential hippocampal activity. 3) In order to identify structure-function relationships, these paradigms will be combined with the high-resolution imaging technology to deliver functional flattened maps of hippocampal activity.

5F31MH011980-02
ZIEGLER, DANA
GLUTAMATERGIC NEUROCIRCUITRY AND STRESS ACTIVATION
UNIVERSITY OF KENTUCKY
LEXINGTON, KENTUCKY

DESCRIPTION (Adapted from applicant's abstract): The central focus of this research proposal is to investigate the neuroanatomy and physiological role of GLUergic neural pathways in the activation the hypothalamic-pituitary-adrenocortical (HPA) axis. The HPA (stress) axis is a neuroendocrine system that is responsible for the adaptation to a wide variety of stressful stimuli, including internal/environmental challenges to homeostasis and social/behavioral stress. HPA axis responses to stress originate in the paraventricular nucleus of the hypothalamus (PVN), which integrates excitatory input from a diverse set of central pathways encoding stressful stimuli. Social/ behavioral types of stress are thought to be conveyed by as yet unidentified pathways emanating from forebrain areas. The neurochemical as well as neuroanatomical identity of such forebrain PVN/HPA-excitatory neural pathways also remains to be determined. Further elucidation of this stress circuitry has major significance for mental health given that deregulation of glucocorticoid secretion has been implicated in the etiology of depressive illness, post-traumatic stress disorder. The specific aims of activation of the PVN and HPA axis responses to stress. Specifically, the proposed experiments are designed to: (1) test the hypothesis that GLUergic innervation of the PVN mediates HPA axis responses to stress, (2) to determine the neuroanatomical origins of GLUergic innervation of PVN, and (3) to test

the hypotheses that chronic stress-induced HPA axis hyperactivity involves enhanced GLUergic input to the PVN.

5F31MH011547-03
ZYLKA, MARK
MOLECULAR ACCESS TO THE MAMMALIAN BIOLOGICAL CLOCK
MASSACHUSETTS GENERAL HOSPITAL
BOSTON, MASSACHUSETTS

DESCRIPTION (Adapted from applicant's abstract): There are a number of human neurobiological disorders that are linked to defects in the circadian timing system. Many of these disorders have been treated effectively with the neuroendocrine hormone melatonin. Circadian effects of melatonin are believed to be mediated by a melatonin receptor subtype (Mel-1a) that is found in the human suprachiasmatic nucleus (SCN). In this research proposal, we will use homologous recombination with the mouse Mel-1a gene locus to target nuclear-localized beta-galactosidase (nlacZ) expression to cells within the SCN. Unlike Mel-1a mRNA, the nlacZ marker can readily be detected at a cellular level. This will facilitate sensitive double-immunocytochemical labeling to determine if cells that express Mel-1a are neurons and/or glia and will be used to determine what neurotransmitters and neuropeptides colocalize in Mel-1a cells. Most importantly, this knock-in strategy will provide us with the ability to determine, at the level of single cells, if the Mel-1a receptor is expressed in SCN neurons that possess an autonomous circadian oscillator. These experiments have the potential of defining and fully characterizing a specific cell type within the mammalian SCN. Additionally, these studies could provide the first molecular tools for accessing the biological clock.